DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-668/S-017

Pfizer Inc.
Attention: Mr. Robert B. Clark
235 East 42nd Street
New York, NY 10017

Dear Mr. Clark:

Please refer to your supplemental new drug application dated August 31, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cardura (doxazosin mesylate) 1, 2, 4, and 8 mg Tablets.

This supplemental new drug application provides for revisions to the package insert (PI) as follows:

1. In the **PRECAUTIONS** section, the following subheading was added following "**Prostate Cancer**":

Cataract Surgery: Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients on or previously treated with other $alpha_1$ blockers. This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs, and potential prolapse of the iris toward the phacoemulsification incisions. The patient's surgeon should be prepared for possible modifications to their surgical technique, such as the utilization of iris hooks, iris dilator rings, or viscoelastic substances. There does not appear to be a benefit of stopping $alpha_1$ blocker therapy prior to cataract surgery.

2. In the **ADVERSE REACTIONS** section, the third paragraph after "TABLE 4 ADVERSE REACTIONS DURING PLACEBO-CONTROLLED STUDIES" was changed from:

In post-marketing experience the following additional adverse reactions have been reported: *Autonomic Nervous System:* priapism; *Central Nervous System:* hypoesthesia; *Endocrine System:* gynecomastia; *Gastrointestinal System:* vomiting; *General Body System:* allergic reaction; *Heart Rate/Rhythm:* bradycardia; *Hematopoietic:* leukopenia, thrombocytopenia; *Liver/Biliary System:* hepatitis, hepatitis cholestatic; *Respiratory System:* bronchospasm aggravated; *Skin Disorders:* urticaria; *Urinary System:* hematuria, micturition disorder, micturition frequency, nocturia.

To:

In post-marketing experience the following additional adverse reactions have been reported: *Autonomic Nervous System:* priapism; *Central Nervous System:* hypoesthesia; *Endocrine System:* gynecomastia; *Gastrointestinal System:* vomiting; *General Body System:* allergic reaction; *Heart Rate/Rhythm:* bradycardia; *Hematopoietic:* leukopenia, thrombocytopenia; *Liver/Biliary System:* hepatitis, hepatitis cholestatic; *Respiratory System:* bronchospasm aggravated; *Skin Disorders:* urticaria; *Special Senses:* Intraoperative Floppy Iris Syndrome (see PRECAUTIONS, Cataract Surgery); *Urinary System:* hematuria, micturition disorder, micturition frequency, nocturia.

We have completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below.

1. In the **PRECAUTIONS** section, the following subheading was added following "**Prostate Cancer**":

Cataract Surgery: Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients on or previously treated with other alpha$_1$ blockers. This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs, and potential prolapse of the iris toward the phacoemulsification incisions. The patient's surgeon should be prepared for possible modifications to their surgical technique, such as the utilization of iris hooks, iris dilator rings, or viscoelastic substances. There does not appear to be a benefit of stopping alpha$_1$ blocker therapy prior to cataract surgery.

This section should read:

Cataract Surgery: Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients on or previously treated with alpha$_1$ blockers. This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs, and potential prolapse of the iris toward the phacoemulsification incisions. The patient's surgeon should be prepared for possible modifications to their surgical technique, such as the utilization of iris hooks, iris dilator rings, or viscoelastic substances. There does not appear to be a benefit of stopping alpha$_1$ blocker therapy prior to cataract surgery.

2. In the **PRECAUTIONS**/**Geriatric Use** section the first sentence was changed from:

The safety and effectiveness profile of CARDURA in BPH was similar in the elderly (age $\geq$ 65 years) and younger (age < 65 years) patients.

To:

The safety and effectiveness profile of CARDURA in BPH was similar in the elderly (age > 65 years) and younger (age < 65 years) patients.

This statement should remain as it was in the previously approved labeling.

3. In the approval letter dated June 13, 2003 for NDA 19-668/S-012 it stated that at the time of the next printing, the storage statement in the **HOW SUPPLIED** section should be changed from:

Recommended Storage: Store below 86° F (30° C).

To:

Store at 25° C (77° F); excursions permitted to 15-30° C (59-86° F)
[see USP Controlled Room Temperature]

This change should be reflected in the final printed labeling (FPL) submitted for this supplement.

The FPL must be identical, and include the minor editorial revisions indicated above, to the submitted labeling (package insert dated August 31, 2005). These revisions are terms of the approval of this application.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that labeling be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper.

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
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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 Melissa Robb, Regulatory Project Manager, at (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 Stockbridge

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