DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

TRANSMITTED VIA FACSIMILE

APR - 2 1999

Rita A. Wittich
Director, Regulatory Affairs
Pfizer Pharmaceuticals
235 East 42nd Street
New York, NY 10017-5755

RE: NDA 19-668, NDA 20-371
Cardura (doxazosin mesylate) tablets
MACMIS ID #7807

Dear Ms. Wittich:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Cardura (doxazosin mesylate) tablets that are in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. DDMAC specifically refers to a journal advertisement (DC098A98) for Cardura that appeared the February 1999, issue of *Urology*. DDMAC objects to this advertisement for the following reasons:

Overstatement of Efficacy

The advertisement includes the prominent claim "Bye-bye BPH symptoms" directly under a large graphic depiction of a men's restroom sign. The graphic depiction portrays the male image from the restroom sign walking away from the sign with one arm extended in what appears to be a goodbye wave. This presentation is misleading because it suggests that patients will no longer experience the symptoms of benign prostatic hyperplasia (BPH) as a result of Cardura therapy. This suggestion overstates the effectiveness of Cardura in treating symptomatic BPH. The approved product labeling (PI) states that clinical studies with Cardura resulted in *improvements* above baseline in both symptoms and maximum urinary flow rate in 66-71% of patients (emphasis added). It has not been demonstrated, however, that Cardura rids patients of symptoms entirely as the ad suggests.

Lack of Fair balance

The advertisement is misleading because it lacks fair balance and minimizes the importance of serious risk information included in the PI for Cardura. Specifically, the PI for this product includes a "WARNINGS" section that is bolded for emphasis. The bolded warning states that Cardura, like other drug in its class, can cause marked hypotension with syncope and other postural symptoms such as dizziness. The warning also explains that marked orthostatic effects

are most common with the first dose, but can also occur with dosage increases or if therapy is interrupted for more than a few days. The warning also states that it is essential that Cardura be initiated with the lowest dose (1 mg) to decrease the likelihood of excessive hypotension or syncope, and that the 2 mg, 4 mg, and 8 mg tablets are not for initial therapy. The warning concludes by explaining that the dose of Cardura should be adjusted slowly, and that patients should be cautioned to avoid situations where injury could result should syncope occur.

The statement "Syncope has been reported, but rarely (<1%)" is included at the bottom of the ad and is the only reference to the information contained in the bolded warning section of the PI. Therefore, the ad is misleading because it minimizes the importance of the information concerning the risk of syncope and marked orthostatic effects. Moreover, the ad fails to present risk information with a prominence and readability reasonably comparable with the presentation of information relating to effectiveness of the drug, taking into account all implementing factors such as typography, layout, paragraphing, white space, and any other techniques apt to achieve emphasis.

In order to address these objections, DDMAC recommends that Pfizer take the following actions:

1. Immediately discontinue the use of these, and all other promotional materials for Cardura that contain the same or similar violations.

2. Provide to DDMAC, in writing, Pfizer's intent to comply with #1 above. Your response should be received by April 16, 1999.

3. This response should include a list of all similarly violative promotional materials and Pfizer's method for discontinuing their use.

If you have any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #7807 in addition to the NDA number.

Sincerely,

/S/

Mark W. Askine, R.Ph.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications