DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

APR - 1 1998

William Baker
Manager, Drug Regulatory Affairs
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877

RE: NDA 20-579
Flomax (tamsulosin HCl) capsules 0.4 mg
MACMIS ID# 6491

Dear Mr. Baker:

Reference is made to Boehringer Ingelheim Pharmaceuticals, Inc.'s (BIPI) February 2, 1998, Form FDA 2253 submission to the Division of Drug Marketing, Advertising, and Communications (DDMAC) for Flomax (tamsulosin HCl). This submission includes a promotional brochure (FL-6504) entitled "Advances in Benign Prostatic Hyperplasia." DDMAC has reviewed this brochure and has determined that it is in violation of the Federal Food, Drug, and Cosmetic Act and the applicable regulations for the following reasons:

Minimizing Significant Risks

"...a drug like tamsulosin will be very promptly embraced by urologists because of the fact that we don't have to worry about affecting a patient's blood pressure..."

"Because tamsulosin has been shown to have little or no cardiovascular impact, it is predicted to be safer and better tolerated among patients with hypertension"

"No clinically significant orthostatic changes"

These claims are false and misleading because they minimize the documented risk of treatment emergent orthostasis in patients treated with Flomax. The WARNINGS section of Flomax's approved product labeling (PI) specifically states "The signs and symptoms of orthostasis (postural hypotension, dizziness, vertigo) were detected more frequently in FLOMAX-treated patients than in placebo recipients. As with other alpha-adrenergic blocking agents, there is a potential risk

of syncope. Patients beginning treatment with FLOMAX should be cautioned to avoid situations where injury result should syncope occur." Furthermore, as is also stated in the PI, dizziness was observed in 15% and 17% of patients taking 0.4 mg and 0.8 mg doses of Flomax, respectively, in clinical trials. Finally, DDMAC is aware of several 10 day adverse event reports for Flomax reporting that patients have experienced symptomatic, and, in some cases, serious, hypotension while taking Flomax.

Unsubstantiated Superiority Claims

"...conventional alpha-blockers have some drawbacks, primarily in terms of tolerability. Dizziness, syncope, asthenia, and somnolence are adverse events associated with alpha-1 blockers...[t]amsulosin may offer significant clinical advantages in this regard."

"When terazosin, doxazosin, and tamsulosin are compared, termination of treatment due to side effects tends to be...least frequent in those patients taking tamsulosin."

"[Flomax's] potentially important safety and tolerability confer advantages over conventional alpha blocker therapy."

These claims are misleading because they suggest that Flomax is superior to other alpha blockers in terms of safety and tolerability without substantial evidence. in the absence of such data, the claims are misleading. Furthermore, these claims also minimize the warning in the PI regarding orthostatic events.

Misleading Quality of Life Claim

The claim "...studies indicate that 70% to 75% of [Flomax] patients can see significant improvement in their [Boyarsky and AUA] symptoms scores, which is a reflection of an improvement in quality of life" is misleading because it suggests, without adequate evidence, that Flomax improves quality of life. There is no evidence that improvements in AUA and Boyarsky symptom scores correlate with improved health related quality of life.

Misleading Pharmacoeconomic Claims

"Flomax offers the following pharmacoeconomic benefits in the treatment of BPH:

- ...Flomax, like other alpha blockers, may delay or obviate the need for expensive inpatient surgery
- ...dose titration is virtually eliminated, which saves time and effort for the physician and reduces the overall cost of care
- ...conferring with other physicians about dosage adjustments with common antihypertensive agents is unnecessary, thus saving additional time, effort, and expense."

These claims are misleading because they suggest, without adequate evidence, that Flomax reduces the overall cost of care in treating patients with BPH.

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

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

2. Provide to DDMAC, in writing, BIPI's intent to comply with #1 above. BIPI's response should be received by April 15, 1998.

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

If BIPI has 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 BIPI that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #6491 in addition to the NDA number.

Sincerely,

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