DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

APR 27 1998

Kathryn Bishburg, Pharm.D.
Associate Director, Regulatory Affairs
Forest Laboratories, Inc.
909 Third Avenue
New York, NY 10022-4731

RE: NDA 50-717
Monurol (fosfomycin tromethamine) Sachet
MACMIS ID # 6461

Dear Dr. Bishburg:

The Division of Drug Marketing, Advertising and Communications (DDMAC), as part of its routine monitoring and surveillance program, has reviewed materials that are used to promote Forest Laboratories, Inc.'s (Forest) product, Monurol. These materials include campus poster (September, 1997), and single dose packaging box (RMC # 3208) submitted on FDA Form 2253. DDMAC finds the dissemination of these promotional pieces to be in violation of the Federal Food, Drug, and Cosmetic Act and the applicable regulations.

Specifically, DDMAC objects to the following:

Efficacy Claims

. **"One Time. One Dose. You're Better.*"**

The above statements, that appear in the campus poster, are misleading because they imply a greater efficacy for Monurol than was demonstrated in the clinical trials used as the basis of approval. Specifically, the size of the presentation, that appears in large type size, and its focus on success with one dose, implies that one dose of Monurol will cure a patient's bladder infection. Although the above statement is linked with an asterisk to the statements "No antibiotic is 100% effective. In controlled clinical trials,

using strict evaluation criteria, almost three quarters of the women were cured after one dose of Monurol," these statements appear in small print at the bottom of the poster. The large type size of the statement "One Time. One Dose. You're Better" overpowers the more specific qualifying information presented at the bottom of the poster.

Untrue or misleading information in any part of a promotion cannot be corrected by the inclusion in another distinct part of the promotion of a brief statement containing true information. Thus, the above statements are misleading.

"No antibiotic is 100% effective...."

The above statement, along with the accompanying overview of the controlled clinical trials for Monurol, is misleading because they fail to reveal material facts regarding the efficacy presentation. Specifically, the poster states the efficacy for Monurol as "almost three quarters of the women were cured after one dose of Monurol," but the poster fails to state the efficacy for the comparator antibiotics. In the clinical trials used as the basis of approval, the comparator antibiotics (ciprofloxacin, trimethoprim/sulfamethoxazole, and nitrofurantoin) demonstrated better efficacy in treating bladder infections. Consequently, by omitting the efficacy rates for the comparator products, Forest is selectively presenting its efficacy information. Further, by omitting this information, Forest fails to disclose that the consequence of a convenient, one dose regimen may be lower effectiveness.

Presentation of Safety Information

The campus poster (September, 97) is misleading because it fails to include adequate risk information associated with the use of Monurol. Promotional materials must present information relating to contraindications, warnings, precautions, and adverse effects with a prominence and readability reasonably comparable with the presentation of information relating to effectiveness. The campus poster contains representations concerning the effectiveness of Monurol, but fails to include an adequate presentation of information about the adverse effects and precautions associated with the use of Monurol.

Specifically, this promotional piece fails to include the information that in addition to diarrhea, vaginitis and nausea, Monurol is associated with other adverse effects that occur at a rate > 1%. The other adverse effects that occur at rates >1% are headache (3.9%), dizziness (1.3%), asthenia (1.1%) and dyspepsia (1.1%). Additionally, this promotional piece fails to include the information, from the Precautions Section of the approved product labeling (PI), that patients should contact their health care provider if their symptoms do not improve in 2 to 3 days.

Single dose packaging box RMC # 3208 is misleading because it fails to provide any information about the adverse events, risks, warnings, or precautions associated with the use of Monurol. Specifically, the statement "Success in a single dose" makes a representation about the effectiveness of the product, and therefore, the box is considered promotional labeling that requires, on its face, fair balance in addition to an accompanying PI.

In order to address these violations, DDMAC recommends that Forest take the following actions:

1. Immediately discontinue the use of the aforementioned materials and any other promotional materials for Monurol that contain the same or similar claims or presentations;

2. Provide a written response to DDMAC of your intent to comply with the above request, and a list of promotional materials containing the misleading presentations that will be discontinued.

Forest's response should be received no later than 10 business days from the issue date of this letter. If Forest 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 Forest that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 6461 in addition to the NDA number.

Sincerely,

Jo Ann Spearmon, M.P.A., Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications