DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL 31 1997

TRANSMITTED VIA FACSIMILE

Foma Rashkovsky
Acting Director, Regulatory Affairs
Forest Laboratories, Inc.
909 Third Avenue
New York, NY 10022-4731

RE: NDA # 50-717
Monurol (fosfomycin tromethamine) Sachet
MACMIS ID# 5544

Dear Mr. Rashkovsky:

Reference is made to Forest Laboratories, Inc.'s (Forest) journal advertisement (SAP #2649) for Monurol that appears in the June 1, 1997, Vol 126, edition of Annals of Internal Medicine and brochure #SAP 2648. The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed the advertisement and promotional labeling and finds them to be in violation of the Federal Food, Drug, and Cosmetic Act and the applicable regulations. Specifically, DDMAC objects to the following claim:

- **"Single-dose clinical efficacy in more than 770 female patients (82% microbiological eradication, 70% clinical success)"**

  This claim is misleading because it fails to reveal material facts in light of the efficacy representation. Specifically, the ad that contains this claim fails to mentioned that the claim is based on a comparative study. It also fails to mention the efficacy rates of the other products used for efficacy comparison in the clinical study, or the efficacy evaluation time points, as stated in the approved product labeling (PI).

  In the pivotal study used as the basis for approval, Monurol was compared to Bactrim, Cipro and Macrobid in controlled, double-blind studies of acute cystitis performed in the United States. Although the studies reported clinical success rates and microbiologic eradication rates for 5 to 11 days and 12 to 21 days post therapy, Forest selected and presented the results for the 5 to 11 days post treatment for Monurol only. Consequently, by

omitting the efficacy and microbiologic eradication rates at the evaluation time points and by only stating the clinical efficacy rates for Monurol at 5 to 11 days post therapy, Forest is selectively presenting its efficacy information.

DDMAC notes that the clinical success rates, demonstrated in the clinical studies used as the basis for approval for Monurol, Bactrim, Cipro, and Macrobid were 70%, 94%, 96%, and 77%, respectively. Additionally, the microbiologic efficacy rates demonstrated by these products at 5 to 11 days post therapy for Monurol, Bactrim, Cipro, and Macrobid were 82%, 98%, 98%, and 76% respectively. Finally, the microbiologic efficacy rated demonstrated by these products at 12 to 21 days post therapy were 77%, 98%, 98%, and 76%, respectively. Thus, by selectively presenting data for Monurol only and by omitting the proper context for the clinical and microbiologic efficacy rates, the claim "Single-dose clinical efficacy in more than 770 female patients (82% microbiological eradication, 70% clinical success)," is misleading.

Further, DDMAC provided extensive comments on this issue in our letter dated March 7, 1997, concerning the proposed submitted launch materials and recommended

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

1. Immediately discontinue the use of the journal advertisement and any other like promotional materials for Monurol that contain the same or similar claims.

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

Forest's response should be received no later than August 15, 1997. 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.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 5544 in addition to the NDA number.

Sincerely,

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