DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

TRANSMITTED VIA FACSIMILE

APR 13 1999

Kathleen J. Day
Director, Labeling and Promotion
Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199

RE: NDA 20-771
Detrol (tolterodine tartrate tablets)
MACMIS ID #7844

Dear Ms. Day:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of a promotional brochure for Detrol, identified as USX 2348.00, that is in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. DDMAC finds this promotional labeling piece, disseminated by Pharmacia & Upjohn (P&U), to be in violation of the Act for the following reasons:

Omission of Material Facts

The brochure includes a presentation concerning the effectiveness of Detrol in reducing the number of urge urinary incontinence episodes. This section of the brochure is preceded by the header "Results of a placebo-controlled clinical trial – change in urge incontinence." Bar graphs representing the decrease in the number of urge incontinence episodes for patients on Detrol and patients on placebo indicate that there was a 50% decrease from baseline in urge incontinence episodes for Detrol patients compared to a 32% decrease for placebo patients. This presentation is misleading because it omits facts material in light of representations concerning the effectiveness of Detrol. Specifically, the difference between the reduction in urge urinary incontinence episodes with Detrol from baseline (-1.2 episodes per 24 hours) and placebo (-0.8 episodes per 24 hours) is not significant. This material fact is not presented in the brochure.

Selectivity Claims

"Detrol - Therapy Selective for overactive bladder"
"Selective for overactive bladder"
"Demonstrates a selectivity for bladder vs salivary glands"
"Exhibits a potent antimuscarinic action on the bladder"
"Greater tissue distribution in bladder vs CNS"

P&U prominently presents these claims either as headlines or in bold type throughout the brochure. Detrol's approved product labeling (PI) states that the drug shows selectivity for the urinary bladder over salivary glands in **cats** (emphasis added). It has not been demonstrated in adequate and well-controlled clinical studies that Detrol is more selective for the bladder in humans. Therefore, these claims and related representations are misleading because they suggest clinical significance when, in fact, no such clinical significance has been demonstrated.

"Easy *bid dosing* – just one 2-mg tablet, twice a day"

This claim, presented on multiple spreads and in the "prescription pad" presentation, is misleading because it lacks important contextual information. Specifically, the PI for Detrol includes precautions concerning the need to reduce the dose in certain patients. Specifically, patients with significantly reduced hepatic function or who are on cytochrome P450 3A4 inhibitors should not receive doses of Detrol greater than 1 mg twice daily. The inclusion of this information on the last page under the header "No titration necessary" does not correct this misleading message.

"New"

DDMAC reminds P&U that claims implying that Detrol is new are misleading because they suggest that the drug was recently cleared for marketing. As you know, Detrol has been available for over one year.

In order to address these objections, DDMAC requests that P&U immediately cease its use of promotional materials that contain these or similar claims or representations. P&U should respond in writing by April 27, 1999, including a list of all similarly violative material and a description of its 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 #7844 in addition to the NDA number.

Sincerely,

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