DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

TRANSMITTED VIA FACSIMILE

APR - 2 1999

Stephen W. Sherman
Director, Advertising and Labeling
Regulatory Affairs
Alza Corporation
1010 Joaquin Road
P.O. Box 7210
Mountain View, CA 94039-7210

RE: NDA 20-897
Ditropan® XL (oxybutynin chloride) Extended Release Tablets
MACMIS ID# 7806

Dear Mr. Sherman:

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 Ditropan XL (oxybutynin chloride) extended release tablets, disseminated by Alza Corporation (Alza), that are in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. DDMAC specifically refers to a promotional file card (0008697) and a direct-to-consumer letter submitted by Alza under cover of Form FDA 2253 on February 23, 1999.

DDMAC has reviewed these promotional labeling pieces and finds them to be in violation of the Act for the following reasons:

Omission of Material Facts

"Clinical studies show that people taking once-a-day Ditropan XL were able to reduce the number of wetting accidents by up to 90%."

This claim, included in the direct-to-consumer letter, is misleading because it omits facts material in light of representations made about Ditropan XL. Specifically, the approved product labeling (PI) for Ditropan XL states that the controlled studies included patients known to be responsive to oxybutynin or other anticholinergic medications. This fact is not disclosed in the direct-to-consumer patient letter. Therefore, the letter is misleading because it fails to convey that the clinical studies were set up to include only patients who the sponsor knew would have improved symptoms on Ditropan XL because they were known to have had improved symptoms on oxybutynin, the active ingredient in Ditropan XL, or other similar medications used to treat overactive bladder. Furthermore, the clinical trial that this claim is derived from, trial C-95-031,

included a placebo arm. In fact, patients randomized to the placebo arm experienced a 51% reduction in the number of wetting accidents. These material facts are also not disclosed in the direct-to-consumer patient letter.

Overstatement of Efficacy

"Help take control...Simply, Confidently."
"Once-a-day confidence."
"...you may be able to go where you want to go and do what you want – without the constant worry of finding a bathroom."

These claims are misleading because they suggest that Ditropan XL is more effective in treating overactive bladder than has been demonstrated. Specifically, patients enrolled in the controlled studies still experienced a mean of 1.5, 4.8, and 2.9 urge incontinence episodes per week at the end of the respective studies. Therefore, these claims suggest a level of efficacy that is not supported by substantial evidence.

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

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

2. Provide to DDMAC, in writing, Alza'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 Alza's method for discontinuing their use.

If Alza 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 Alza that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID 7806 in addition to the NDA number.

Sincerely,

/S/

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