DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FOI

Food and Drug Administration
Rockville MD 20857

MAY 29 1997

TRANSMITTED VIA FACSIMILE

Aruna Dabholkar, M.D.
Regulatory Products Manager
TAP Holdings, Inc.
Bannockburn Lake Office Plaza
2355 Waukegan Road
Deerfield, Illinois 60015

RE: **NDA#** 20-517
Lupron Depot (leuprolide acetate)
MACMIS ID #5439

Dear Dr. Dabholkar :

As part of its routine monitoring and surveillance procedures, the Division of Drug Marketing, Advertising and Communications (DDMAC) has become aware of promotional material for Lupron Depot (leuprolide acetate) that is in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and applicable regulations.

Specifically, DDMAC is in possession of a letter bearing TAP Holdings, Inc (TAP) letterhead dated February 25, 1997, from Carl Agre, M.D. to David P. Sheridan, M.D., M.S., Medicare Medical Director. In the letter, Dr. Agre, Director of Medical Affairs for TAP, makes the following claims:

1. "Lupron Depot's delivery systems fall well within the standard practice of nurses and physicians....Zoladex's delivery system requires special training, and, in many cases, the application of a local anesthetic."

This claim is misleading because it lacks contextual information, and is an unsubstantiated superiority claim. As stated in Zoladex's approved labeling, "A local anesthetic may be used in the normal fashion at the option of the administrator or patient." The delivery system does not require the use of a local anesthetic for administration. Further, Zoladex administration does not require special training and does fall well within the standard practice of nurses and physicians.

2. "One of these clinical difference between Lupron Depot and Zoladex is testosterone suppression levels." "While not directly comparable to the Lupron

Depot trials, they (Zoladex trials) indicate a higher incidence of testosterone escapes and acute on chronic events."

These claims are misleading because they suggest that Lupron has a lower incidence of testosterone escapes and a better adverse event profile than Zoladex without substantiation from head to head comparative trials.

3. "...the Zoladex Summary Basis of Approval raises concerns as to whether or not the one and three month formulations of Zoladex are equivalent."

This claim is misleading because it is inconsistent with the PI for Zoladex, which states, " In controlled clinical studies of patients with advanced prostatic cancer, Zoladex 10.8 mg implant produced pharmacodynamically similar effect in terms of suppression of serum testosterone to that achieved with Zoladex 3.6 mg implant. Clinical outcome similar to that produced with the use of the Zoladex 3.6 mg implant...is predicted with the Zoladex 10.8 mg implant..."

4. "It is unclear if the Zoladex 3-month product will ever be approved for a female indication in which suppression of estradiol is required...Tap has also studied Lupron Depot 3-month in endometriosis and currently has an application before the FDA...at a dosage strength of 11.25 mg, half the strength of that administered for prostate cancer."

This claim is misleading because it implies superiority for gynecological indications in the absence of head to head studies. Further, the gynecological indications for these products have no bearing on the superiority of Lupron over Zoladex in the treatment of prostate cancer.

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

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

2. Provide to DDMAC, in writing, TAP's intent to comply with #1 above. TAP's response should be received by June 12, 1997.

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

If TAP 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 TAP that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #5439 in addition to the NDA number.

Sincerely,

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