DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Henry Pietraszek

Ma

March 9, 1990
President
TAP Pharmaceuticals
1400" Sheridan Road
North Chicago, Illinois 60064

Dear Mr. Pietraszek:

This is in reference to the comparative promotion of Lupron brand products under NDAs 19-732 and 19-010. The matters discussed below have come to our attention through an industry complaint.

We have been provided with a copy of a document alleged to be a sales aid in use by your firm's representatives. This sales aid is multiply violative and, if in use by your firm, causes your Lupron products to be misbranded under section 502(a) of the Federal Food, Drug and Cosmetic Act. We have enclosed a copy of this document for your use in investigating this complaint.

Violations presented in the document include false and/or misleading statements regarding the competing Zoladex product, as well as unfair characterizations of both products thereby creating the impression of superiority of Lupron which impression is not supported by adequate and well-controlled studies designed to show such differences. The violations are delineated below.

1 - Under the approved labeling for both products, there is no greater need to observe Zoladex patients for allergic reactions than with Lupron. In fact, the labeling for both drugs lists an identical statement in the Contraindications section regarding anaphylaxis. Prudent medical practice would dictate the same amount of care for either implantation of Zoladex or repository injection of Lupron Depot.

It is false and/or misleading to represent and/or suggest that a difference exists.

2 - We are unaware of evidence which suggests that administration of Lupron Depot is any less painful or locally irritating than implantation of Zoladex. In fact, the app-roved labeling for Lupron Depot lists the possibility of "dermatitis and local skin reactions" at less than 5% which is probably equivalent to the statement in the Zoladex labeling that "only 3% of Zoladex patients reported adverse reactions at the injection site." Therefore, it is false and/or misleading to suggest that there is a difference in the propensity for either product to cause pain upon administration. Furthermore, use of a local anaesthetic is listed as optional with Zoladex. It is not a requirement, as is suggested by the attached document.

3 - We are similarly unaware of any reason for which either product would be more or less prone to causing abscess formation. Both products are repository injections. It is false and/or misleading to represent or suggest that either product is safer in this regard.

4 - We are unaware of any reason which would require viewing of a video or any other training which would be different between the two products. Training is necessary for the proper administration of intramuscular injections as well as for subcutaneous implants. It is false and/or misleading to represent and/or suggest that either product is safer by virtue of such a difference.

5 - There is nothing in the approved labeling for Zoladex to suggest that an increase in dosage is ever required. Furthermore, the onset of therapeutic action is characterized identically for Zoladex and for Lupron. That is, castrate testosterone levels are reached two to four weeks following initiation of therapy. It is false and/or misleading to represent and/or suggest any difference between the two products with respect to these parameters.

6 - The adverse reactions profile of both drugs is similar. It is false and/or misleading to represent and/or suggest any significant difference between the two drugs in this regard.

7 - In the absence of head-to-head clinical comparisons of appropriate design, it is false and/or misleading to state

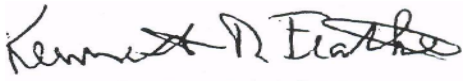
that the survival rate of Lupron is equal to that of any other drug. The efficacy of Lupron may only be compared to other products or treatments against which it has received adequate clinical trial.

8 - It is false and/or misleading to make cost comparisons on the basis of "probable" data.

9 - It is false and/or misleading to represent and/or suggest that an actual expense to individual patients is JLn any way mitigated by a "compassionate" program unless this program actually accomplishes such a price reduction to all such patients. In other words, if the net expense of Lupron is higher to some patients than other treatments, regardless of the reason - e.g. differences in reimbursement schemes, then it is more expensive to those individuals regardless of price reductions or even free provision to other individuals.

We request your written response within fifteen (15) working days of receipt of this letter indicating the steps you have taken to investigate these charges. If your investigation indicates that this promotional material has been disseminated by or on behalf of your firm, then your response should also include the steps you have taken to 1) correct the situation to prevent recurrence, and 2) remove this and any other similar or related violative promotional materials from all channels of distribution down to the recipients. Because of the seriously violative nature of this material, a simple "pro forma" explanation that this was the action of a "rogue" detail person will not be sufficient. A more detailed investigation of your field sales force, and supporting evidence thereof, is requested.

Sincerely yours,



Kenneth R. Feather
Acting Director
Division of Drug
Advertising
and

Labeling
Office of
Drug
Standards
TAP

Enclosure

Pharmaceuticals	TAP Pharmaceuticals

Lupron Depot

HFA-224 HFD-200
HFD-240(Chron)
HFD - 244 (Count)

HFD-244 (Lupron File/Takeda- Abbott R&D , dba TAP Pharmaceuticals)
HFD-510(NDA 19-010 and 19-732) HFD-510(Dr. Fourcroy) AKYellin:3/8/90:lupcompl.ltr:els
revised per direction of KRFeather: 3/9/90