DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV - 7 1997

TRANSMITTED BY FACSIMILE

Ms. Linda Peters
Senior Regulatory Products Manager
TAP Holdings, Inc.
Bannockburn Lake Office Plaza
2355 Waukegan Rd.
Deerfield, IL 60015

Re: **NDA 20-406**
Prevacid (lansoprazole) Delayed-Release Capsules
MACMIS ID #5869

Dear Ms. Peters:

This letter is in reference to TAP Pharmaceutical's (TAP) submissions dated July 15, 1997, and September 29, 1997, of promotional materials under cover of Form FDA 2253 for Prevacid (lansoprazole) Delayed-Release Capsules. One submission consisted of a promotional brochure identified as P97-1808, while another submission consisted of a brochure highlighting a slide presentation identified as P97-1709. The Division of Drug Marketing, Advertising, and Communications (DDMAC) regards these materials to be false or misleading under the Federal Food, Drug, and Cosmetic Act and regulations promulgated thereunder. Specific objections to these promotional materials are presented below.

Misleading Product Comparisons

On page 7 in brochure P97-1808, TAP presents the results of a study comparing the efficacy of lansoprazole to an active control in the treatment of erosive esophagitis and states that lansoprazole provides the symptom relief at week 2 that an active control provides at week 8. However, the approved product labeling for lansoprazole states that the studies comparing the efficacy of lansoprazole and the active control (ranitidine) do not represent an adequate comparison with ranitidine because the dose of the active control used in the comparative studies was one half of the recommended dose. Therefore, the implication that lansoprazole provides quicker or faster symptom relief than the active control is false or misleading.

TAP also implies that lansoprazole is superior to ranitidine by comparing the results of studies that evaluated these drugs in the treatment of erosive esophagitis. Specifically, TAP contrasts the healing rates in erosive esophagitis for lansoprazole on page 8 with the healing rates in erosive esophagitis for ranitidine on page 9. This presentation implies that lansoprazole provides faster

healing than ranitidine. Substantial evidence required to support this comparative claim would be from adequate, well-controlled, head-to-head studies. However, this comparison is from different studies and is not adequate to support the claim. Therefore, this claim is false or misleading.

TAP then states on page 9 that lansoprazole "provides healing of erosive esophagitis at week 2 that is similar to the healing rates provided by an active control at week 8." This statement and accompanying graphic are derived from the approved product labeling, but as stated above, this study does not represent an adequate comparison with ranitidine because the dose of ranitidine used in this study is half of the currently recommended dosage for ranitidine in the treatment of erosive esophagitis. Therefore, when presented in this context, the presentation is misleading.

False and Misleading Statements Concerning Competitive Products

Similarly, in slides 18 and 24 in brochure P97-1709, TAP presents statements concerning the use of cisapride in patients with mild to moderate symptoms of GERD and maintenance of healed GERD. However, the approved product labeling for cisapride states that it "is indicated for symptomatic treatment of patients with nocturnal heartburn due to gastroesophageal reflux disease." Therefore, these statements are inconsistent with the approved product labeling for cisapride. False and misleading representations with respect to a competitive drug may render Prevacid misbranded.

Misleading Data Presentations

On the second page of brochure P97-1808, TAP states that acid exposure is an important factor in the degree and duration of erosive esophagitis. TAP further states in large letters with accompanying graphics that lansoprazole suppresses gastric acid more effectively than omeprazole. On the next page, TAP states that lansoprazole suppresses gastric acid longer than omeprazole. Then in small type size at the bottom of each page, combined with other information, TAP discloses that the "correlation between intragastric pH and healing is unknown." DDMAC previously objected to proposed claims concerning this issue in letters dated March 24, 1997 and April 17, 1997. DDMAC reviewed TAP's arguments and data submitted to support these claims in TAP's letter dated October 22, 1997. As stated in our letter dated November 7, 1997, we are not persuaded and maintain our objections to these claims.

In a letter dated July 24, 1996, DDMAC objected to TAP's use of a meta-analysis comparing proton pump inhibitors and H_2-receptor antagonists because the data were not derived from head-to-head clinical trials and the presentation was considered false or misleading. In another letter dated August 21, 1996, DDMAC objected to the use of materials which made product comparisons between lansoprazole and ranitidine because the dose of ranitidine used in the

comparison was half of the recommended dosage. Thus, DDMAC is concerned that TAP is continuing to present these violative claims.

TAP should immediately suspend all promotional activities and materials that convey or contain the allegedly violative claims or information identified in this letter until these allegations are resolved. TAP should submit a written response to DDMAC on or before November 24, 1997, describing the steps that it has taken to ensure that the use of these materials have been suspended and to ensure that such violations will not occur again.

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.

Please reference MACMIS ID #5689 in addition to the NDA number in future correspondence concerning this issue.

Sincerely,

Stephen W. Sherman, MBA
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications