DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

NOV - 2 1999

Lewis Pollack, Ph.D.
Director, Regulatory Affairs
Nabi
12280 Wilkins Avenue
Rockville, MD 20852

RE: NDA 20-298
Aloprim™ (allopurinol sodium) for Injection
MACMIS ID# 8402

Dear Dr. Pollack:

Reference is made to your 2253 submission dated August 16, 1999, which contains a Sales Visual Aid (sales aid) for Aloprim (allopurinol sodium) for Injection. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has determined that this promotional piece is in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and its implementing regulations. DDMAC requests that the use of the above referenced material and those containing similar promotional claims cease immediately.

Overstatement of Efficacy

- The sales aid makes claims that Aloprim "*controls* uric acid levels which have been linked to renal complications." The word "controls" implies the drug is more effective than has been demonstrated by substantial evidence. Furthermore, the phrase suggests that Aloprim can decrease renal complications by decreasing uric acid levels. However, the approved product labeling (APL) states that, "Because of the study design, it was not possible to assess the impact of the treatment upon the clinical outcome of the patient groups."

- The sales aid contains graphs that depict prophylactic and therapeutic results in adult and pediatric patients. This information suggests that Aloprim was effective in achieving normal or reduced serum uric acid levels in 88% of adult and 95% of pediatric patients in clinical trials. However, the APL lists different results (68% of patients with established hyperuricemia achieved normal levels; 93% achieved reduced levels). Nabi's presentation is inconsistent with the labeling and suggests that the drug is more effective than has been demonstrated by substantial evidence or clinical experience; therefore, the graphs are misleading.

Lack of Fair Balance

- An advertisement may be lacking in fair balance if it fails to present information relating to side effects and contraindications with a prominence and readability reasonably comparable with the presentation of information relating to effectiveness of the drug, taking into account all implementing factors such as typography, layout, contrast, headlines, paragraphing, white space, and any other techniques apt to achieve emphasis. Throughout the sales aid, the presentation of important risk information is minimized. For example, in contrast to emphasis given to claims for the drug, contraindications and warnings are placed in smaller font in paragraph form without a header at the bottom of the page which is titled, "Aloprim - Appropriate Therapy for a Variety of Oncology Patients." Information on drug interactions and important dosage adjustments that are required when Aloprim is administered concomitantly with mercaptopurine or azathioprine is placed as an unbolded footnote on a separate page distant from the recommended dosing parameters. Furthermore, throughout this eight-page sales aid, only one section (e.g., most frequent adverse events) prominently displays the risk information. The sales aid makes use of colors and graphs to prominently display efficacy information but does not display contraindications and warnings with reasonably comparable prominence; therefore, the sales aid is lacking in fair balance, in violation of the Act and its implementing regulations.

We request that the distribution and use of this sales aid as well as other similarly violative promotional pieces cease immediately. You should submit in writing, on or before November 16, 1999, a list of materials that will be discontinued and a description of the steps that you will take to comply with the above request.

You should direct your response to me by facsimile at (301) 594-6771, or by written communication to the Division of Drug Marketing, Advertising, and Communications, HFD-42; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. We remind you that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS ID# 8402 and NDA 20-298.

Sincerely,

/S/

Jean-Ah Choi, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications