DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FDA

Food and Drug Administration
Rockville MD 20857

JUN 25 1997

**TRANSMITTED VIA FACSIMILE**

Anne S. Davidson
Vice President and Associate General Counsel
Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover, New Jersey 07936-1080

**RE: NDA#** 20-313
**Miacalcin Nasal Spray (calcitonin salmon)**
MACMIS ID # 5521

Dear Ms. Davidson:

This letter is in reference to Sandoz Pharmaceuticals' (Sandoz) November 20, 1997, FDA Form 2253 submission for Miacalcin. This material includes the reprint and reprint carrier titled "Intranasal Salmon Calcitonin for the Prevention and Treatment of Postmenopausal Osteoporosis" by Ellerington et al. (#MNS8041). Reference is also made to the May 29, 1997, teleconference between Ms. Davidson and Ms. Reb. During this teleconference, Ms. Davidson indicated that these materials are still in use.

Ms. Davidson also indicated that the June 28, 1996, FDA Form 2253 submission of a reprint carrier (#MNS-8035) and reprint ("Effect of salcatonin (Miacalcin) given intranasally on bone mass and fracture rates in established osteoporosis: a dose-response study" by Overgaard et al.) are no longer in print.

The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed these materials and finds that they are misleading and in violation of the Federal Food, Drug, and Cosmetic Act. Specifically, DDMAC objects to the following:

Indication

The reprint and reprint carrier are misleading because they lack fair balance and imply that Miacalcin is useful in a broader range of patients than indicated. For example, the headlines on the outside and inside cover of the reprint carrier ("Intranasal Salmon Calcitonin for the Prevention and Treatment of Postmenopausal Osteoporosis") suggest that Miacalcin is indicated for the prevention of osteoporosis. However, Miacalcin is

indicated only for the treatment of osteoporosis in a limited population, as discussed in the approved product labeling:

> "for the treatment of postmenopausal osteoporosis in females greater than 5 years post-menopause with low bone mass relative to healthy premenopausal females. Miacalcin Nasal Spray should be reserved for patients who refuse or cannot tolerate estrogens or in whom estrogens are contraindicated. Use of Miacalcin is recommended in conjunction with an adequate calcium and vitamin D intake to retard the progressive loss of bone mass."

Study Results

The presentation of study results is misleading because it selectively presents benefit information and fails to provide adequate context for the study findings. For example, Novartis states that "the late postmenopausal subgroup showed the greatest response to treatment, with a total increase in BMD of the lumbar spine of 1.4%..." and "patients in the placebo group experienced significant bone loss in the spine and the proximal femur." However, Novartis fails to present the results for the early postmenopausal patients:

. lumbar spine bone loss continued in all treatment groups

. the rates of femoral neck bone loss in those receiving placebo and those receiving daily calcitonin were similar.

The results in this subgroup would be important to communicate because they provide information about the population eligible for therapy.

Risk Information

The risk and warning information presented in a footnote on the back cover is not reasonably comparable to the presentation of benefit information.

Further, the discussion of side effects is misleading because it minimizes the significance of the nasal events due to the product. For example, Sandoz states, "Miacalcin Nasal Spray therapy was well-tolerated; patients reported a variety of minor adverse events comparable between treatment groups." However, Sandoz fails to present the incidence rates for adverse events for Miacalcin versus placebo; i.e., nasal events 34% and 24% and rhinitis 23% versus 7% respectively.

Therefore, DDMAC requests that Sandoz immediately discontinue the dissemination and use of these materials and all other promotional materials with similar issues. DDMAC requests that

Novartis submit a written response indicating your intent to comply with this request by July 10, 1997.

If Novartis has any questions or comments, please contact me 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.

In all future correspondence regarding the materials discussed in this letter, please refer to MACMIS ID #5521 in addition to the NDA number.

Sincerely,

Anne M. Reb, NP
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications