DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

OCT 27 1997

Gregory M. Torre, Ph.D., J.D.
Senior Director
Medical Affairs, 6th floor
Sanofi Pharmaceuticals, Inc.
90 Park Avenue
New York, NY 10016

RE: **NDA#** 19-436
Primacor (milrinone lactate injection)
MACMIS ID# 5800

Dear Mr. Torre:

As part of its routine monitoring program, the Division of Drug Marketing, Advertising and Communications (DDMAC) has become aware of promotional materials for Primacor (milrinone lactate injection) by Sanofi Pharmaceuticals, Inc. (Sanofi) that violate the Federal Food, Drug and Cosmetic Act and its regulations. Reference is made to brochures 60-611230B and 60-610000A, submitted under cover of Form FDA 2253. DDMAC has reviewed these brochures and has determined that they promote Primacor for unapproved uses, or are otherwise misleading.

In brochure 60-611230B, Sanofi presents a case study in which the patient is treated as an inpatient with Primacor, and is subsequently discharged with the follow-up therapy to include trying "a series of weekly outpatient infusions of milrinone in order to prevent fluid reaccumulation, worsening symptoms, and worsening renal function." The treatment rationale states that "[b]rief intermittent outpatient inotropic infusions achieve many goals for patients who cannot stay at their 'dry weight' with conventional medications (which may further impair renal function)." DDMAC considers that these statements imply that Primacor is indicated for intermittent, prophylactic, outpatient infusion for the prevention of worsening congestive heart failure. However, the approved product labeling for Primacor states that Primacor is only indicated for the short-term intravenous therapy of congestive heart failure. Therefore, to suggest that Primacor is indicated for intermittent, prophylactic therapy is inconsistent with the approved product labeling and is false and/or misleading.

In addition, Sanofi uses the term "outpatient" without defining what constitutes an appropriate outpatient setting for Primacor therapy. Without context, DDMAC is concerned that this could be interpreted as "home" infusion therapy. Several cardiovascular events, including

arrhythmias, have been associated with Primacor's use. The approved product labeling for Primacor clearly states that "patients receiving Primacor should be closely monitored during infusion." Therefore, the claim for use of Primacor as outpatient therapy, without defining the limits and precautions of such therapy, is lacking in fair balance, or otherwise misleading. In addition, the disclaimer appearing at the bottom of the brochure is neither prominent in placement, nor adequate in context to balance this claim.

In brochure 60-610000A, Sanofi presents a case study in which Primacor is used to evaluate a patient for establishing candidacy for heart transplant. This indication is also inconsistent with the approved product labeling for Primacor, and therefore, promotes Primacor for an unapproved use.

Sanofi should immediately cease distribution of these and other similar promotional materials for Primacor that contain the same or similar claims or presentations. Sanofi should submit a written response to DDMAC on or before November 10, 1997, describing its intent and plans to comply with the above.

Sanofi should direct its response to 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 Sanofi that only written communications are considered official.

In all future correspondence regarding this particular matter please refer to MACMIS ID #5800 in addition to the NDA number.

Sincerely,

Janet Norden, MSN, RN
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications