

NDA 20-912/S-007  
NDA 20-913/S-006

23 MAR 2001

Merck Research Laboratories  
Attention: Michael C. Elia, Ph.D.  
Sumneytown Pike, P.O. Box 4  
BLA-20  
West Point, PA 19486

Dear Dr. Elia:

Please refer to your supplemental new drug applications dated September 14, 2000, received September 15, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aggrastat (tirofiban hydrochloride) Injection and Aggrastat (tirofiban hydrochloride) Premixed Injection.

These "Changes Being Effected" supplemental new drug applications provide for revisions to the **PRECAUTIONS** and **ADVERSE REACTIONS** sections of the package insert. The **PRECAUTIONS/Bleeding Precautions/Laboratory Monitoring** subsection has been revised to include additional information on the anticoagulant effects of heparin. The **ADVERSE REACTIONS/Post-Marketing Experience** subsection has been revised to include additional information on bleeding based on post-marketing adverse events reports.

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in your September 14, 2000 submitted labeling, with the minor revisions you agreed to in your March 5, 2001 telephone conversation with Ms. Colleen LoCicero, Regulatory Health Project Manager, Division of Cardio-Renal Drug Products, as listed below. Accordingly, these supplemental applications are approved effective on the date of this letter.

1. Please revise the last sentence in the section on bleeding in the **ADVERSE REACTIONS/Post-Marketing Experience** subsection from the following:

Fatal bleedings have been reported rarely.

to the following:

Fatal bleeding events have been reported.

The final printed labeling (FPL) must be identical, and include the minor revisions indicated, to the September 14, 2000 submitted package insert. These revisions are terms of the approval of these applications.

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 20-912/S-007, 20-913/S-006." Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Ms. Colleen LoCicero  
Regulatory Health Project Manager  
(301) 594-5332

Sincerely,

{See appended electronic signature page}

Raymond J. Lipicky, M.D.  
Director  
Division of Cardio-Renal Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research