# CENTER FOR DRUG EVALUATION AND RESEARCH

**Application Number: NDA 20-912/S001**

## APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUL – 9 1999

NDA 20-912/S-001
NDA 20-913/S-001

Merck Research Laboratories
Attention: Jeffery R. White, M.D.
Sumneytown Pike, P.O. Box 4
BLA-20
West Point, PA 19486

Dear Dr. White:

Please refer to your supplemental new drug applications dated October 16, 1998, received October 21, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aggrastat (tirofiban hydrochloride) Injection, 12.5 mg per 50 ml vial (NDA 20-912) and Aggrastat (tirofiban hydrochloride) Premixed Injection, 25 mg per 500 ml single-dose container (NDA 20-913).

We acknowledge receipt of your submissions dated February 12, and May 19, 1999.

These supplemental new drug applications provide for changes to the **CLINICAL PHARMACOLOGY** and **DOSAGE AND ADMINISTRATION** sections of the labeling as follows:

1. has been changed to "controlled" in the first sentence of the second paragraph following Table 2 in the *Clinical Trials*/**CLINICAL PHARMACOLOGY** subsection, because it is redundant.

2. The last sentence of the *Precautions*/**DOSAGE AND ADMINISTRATION** subsection has been changed from the following:

   to the following:

   Any unused solution should be discarded.

3. The first sentence in the second paragraph of the *Directions for Use*/**DOSAGE AND ADMINISTRATION** subsection has been changed from the following:

to the following:

> AGGRASTAT Injection Premixed is supplied as 500 mL of 0.9% sodium chloride containing 50 µg/mL tirofiban.

4. The following sentence has been added as the last paragraph of the *Directions for Use*/**DOSAGE AND ADMINISTRATION** subsection:

> AGGRASTAT may be administered in the same intravenous line as dopamine, lidocaine, potassium chloride, and PEPCID* (famotidine) Injection.

The May 19, 1999 submitted final printed labeling is identical to the October 16, 1998 submitted draft labeling, as was requested by the Agency in our March 23, 1999 approvable letter, with an exception. Changes to the **ADVERSE REACTIONS** section that were submitted on February 17, 1999 as 'Special Supplements-Changes Being Effected' and subsequently approved on June 9, 1999 are also included in the May 19, 1999 submitted final printed labeling.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the submitted final printed labeling (package insert submitted May 19, 1999). Accordingly, these supplemental applications are approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" 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 contact:

Colleen LoCicero
Regulatory Health Project Coordinator
(301) 594-5312

Sincerely yours,

/S/ 7/9/99

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

# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER: NDA 20-912/S001

## APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-912/S-001
NDA 20-913/S-001

MAR 23 1999

Merck Research Laboratories
Attention: Larry P. Bell, M.D.
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Bell:

Please refer to your supplemental new drug applications dated October 16, 1998, received October 21, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aggrastat (tirofiban hydrochloride) Injection, 12.5 mg per 50 ml vial (NDA 20-912) and Aggrastat (tirofiban hydrochloride) Premixed Injection, 25 mg per 500 ml single-dose container (NDA 20-913).

We acknowledge receipt of your submissions dated February 12, 1999.

These supplemental applications provide for draft labeling revised under the **CLINICAL PHARMACOLOGY** and **DOSAGE AND ADMINISTRATION** sections as follows:

1. has been changed to "controlled" in the first sentence of the second paragraph following Table 2 in the *Clinical Trials*/**CLINICAL PHARMACOLOGY** subsection, because it is redundant.

2. The last sentence of the *Precautions*/**DOSAGE AND ADMINISTRATION** subsection has been changed from the following:

   to the following:

   Any unused solution should be discarded.

3. The first sentence in the second paragraph of the *Directions for Use*/**DOSAGE AND ADMINISTRATION** subsection has been changed from the following:

   to the following:

   AGGRASTAT Injection Premixed is supplied as 500 mL of 0.9% sodium chloride containing 50 $\mu$g/mL tirofiban.

4. The following sentence has been added as the last paragraph of the *Directions for Use*/**DOSAGE AND ADMINISTRATION** subsection.

   AGGRASTAT may be administered in the same intravenous line as dopamine, lidocaine, potassium chloride, and PEPCID* (famotidine) Injection.

We have completed the review of these applications, as amended, and they are approvable. Before these applications may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for these drugs. The labeling should be identical in content to the October 16, 1998 submitted draft labeling.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submissions, please provide a highlighted or marked-up copy that shows the changes that are being made.

Please submit 20 copies of the final printed labeling, ten of which are individually mounted on heavy weight paper or similar material to each application.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the supplemental applications, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the applications. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, please contact:

Ms. Colleen LoCicero
Consumer Safety Officer
(301) 594-5312

Sincerely yours,

/S/ 3/23/99

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