



NDA 20-913/S-009

NDA 20-912/S-012

Merck & Co., Inc.
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 September 5, 2001 supplemental new drug applications, received September 6, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aggrastat (tirofiban hydrochloride) Premixed Injection and Aggrastat (tirofiban hydrochloride) Injection.

These "Changes Being Effected" supplemental new drug applications provide for the removal from the **DESCRIPTION, DOSAGE AND ADMINISTRATION**, and **HOW SUPPLIED** sections of the package insert of language pertaining to the 500 mL bag that is no longer marketed. Additionally, language regarding "spinal-epidural hematoma" based on post-marketing adverse event reports has been added to the **PRECAUTIONS** and **ADVERSE REACTIONS** sections.

These changes are as follows:

1. The first sentence of the fifth paragraph of the **DESCRIPTION** section was revised from the following:

AGGRASTAT Injection Premixed is supplied as a sterile solution in water for injection, for intravenous use only, in plastic containers of 250 mL or 500 mL.

to the following:

AGGRASTAT Injection Premixed is supplied as a sterile solution in water for injection, for intravenous use only, in plastic containers of 250 mL.

2. The last sentence of the fifth paragraph of the **DESCRIPTION** section that contained information pertaining to the 500 mL bag was deleted.
3. The first sentence of the **PRECAUTIONS/Bleeding Precautions/Minimize Vascular and Other Trauma** subsection was revised from the following:

Other arterial and venous punctures, intramuscular injections, and the use of urinary catheters, nasotracheal intubation and nasogastric tubes should be minimized.

to the following:

Other arterial and venous punctures, epidural procedures, intramuscular injections, and the use of urinary catheters, nasotracheal intubation and nasogastric tubes should be minimized.

4. The **ADVERSE REACTIONS/Post-Marketing Experience/Bleeding** subsection was revised from the following:

Bleeding: Intracranial bleeding, retroperitoneal bleeding, hemopericardium and pulmonary (alveolar) hemorrhage. Fatal bleedings have been reported rarely;

to the following:

Bleeding: Intracranial bleeding, retroperitoneal bleeding, hemopericardium, pulmonary (alveolar) hemorrhage, and spinal-epidural hematoma. Fatal bleeding events have been reported;

5. The first sentence of the second paragraph of the **DOSAGE AND ADMINISTRATION/Directions for Use** subsection was revised from the following:

AGGRASTAT Injection Premixed is supplied as 250 mL or 500 mL of 0.9% sodium chloride containing 50 mcg/mL tirofiban.

to the following:

AGGRASTAT Injection Premixed is supplied as 250 mL of 0.9% sodium chloride containing 50 mcg/mL tirofiban.

6. The text in the **HOW SUPPLIED** section pertaining to the premixed injection was revised from the following:

No. 3739 – AGGRASTAT Injection Premixed 12.5 mg tirofiban per 250 mL (50 mcg per mL) and 25 mg tirofiban per 500 mL (50 mcg per mL) are clear, non-preserved, sterile solutions premixed in a vehicle made iso-osmotic with sodium chloride, and are supplied as follows:

NDC 0006-3739-96, 250 mL single-dose IntraVia® containers (PL 2408 Plastic).

to the following:

No. 3739 – AGGRASTAT Injection Premixed 12.5 mg tirofiban per 250 mL (50 mcg per mL) is a clear, non-preserved sterile solution premixed in a vehicle made iso-osmotic with sodium chloride, and is supplied as follows:

NDC 0006-3739-96, 250 mL single-dose IntraVia® containers (PL 2408 Plastic).

7. Your address was revised from the following:

MERCK & CO., INC.
West Point, PA 19486, USA

to the following:

MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA

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 the submitted final printed labeling (package inserts submitted September 5, 2001). 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 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}

Douglas C. Throckmorton M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Doug Throckmorton
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