DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 20-718/S-002

SEP 2 0 1999

COR Therapeutics, Inc.
Attention: Ms. Ellen L. Martin
256 East Grand Avenue
South San Francisco, CA 94080

Dear Ms. Martin:

Please refer to your supplemental new drug application dated October 9, 1998, received October 13, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Integrilin (eptifibatide) Injection, 20 mg/10 mL and 75 mg/100 mL Vials.

We acknowledge receipt of your submission dated August 20, 1999 that constituted a complete response to our August 9, 1999 action letter.

This supplement provides for final printed labeling revised to include information describing the PURSUIT six-month follow-up data.

Your original October 9, 1998 submission proposed the following labeling changes:

1. The reference to Figure 1 was deleted in the paragraph immediately preceding Table 2 in the **CLINICAL STUDIES** section.

2. Figure 1 in the **CLINICAL STUDIES** section was revised to include the six-month PURSUIT data and moved so that it immediately preceded the discussion of the IMPACT II study in the **CLINICAL STUDIES** section. In addition, the following paragraph was added to precede Figure 1 immediately:

   A secondary endpoint of the study was the occurrence of death from any cause or new myocardial infarction (as reported by investigators) within 6 months of randomization. As shown in the Kaplan-Meier curve in Figure 1, investigators reported a reduction in death or MI from 13.6% with placebo to 12.1 % with eptifibatide (p=0.021 log rank) within 6 months of randomization.

3. The following paragraph regarding the assessment of stroke at six months was inserted between the first and second paragraphs of the **ADVERSE REACTIONS/Intracranial Hemorrhage and Stroke** subsection:

   Investigator's assessment of all strokes within 6 months of randomization was 0.8% in patients receiving eptifibatide 180/1.3, 1.3% in patients receiving eptifibatide 180/2.0, and 1.5% in placebo patients.

In our May 4, 1999 approvable letter for this supplement, we noted that this application was approvable, provided the following changes were made:

1. Figure 1 remained as it was in the approved labeling and was not revised or relocated. The reference to Figure 1 in the current text remained, as well.

2. The revised Figure 1 and the paragraph proposed to precede the revised Figure 1 immediately were not included in labeling, as they were not acceptable. We asked you to provide the five-month endpoint data for the PURSUIT study, noting that after the five-month data were reviewed by the Division, a determination would be made as to how this might be included in labeling.

3. The paragraph regarding the assessment of stroke at six months that was inserted between the first and second paragraphs in the **ADVERSE REACTIONS/Intracranial Hemorrhage and Stroke** subsection was not included in labeling, as it was not acceptable.

In your May 7, 1999 submission you concurred with all of the labeling changes specified in the May 4, 1999 approvable letter, with one exception. You proposed to add the following paragraph to the **CLINICAL STUDIES** section of the package insert, immediately preceding the IMPACT II study description:

> A secondary endpoint of PURSUIT was the occurrence of death from any cause or new myocardial infarction (as reported by the investigators) within 6 months of randomization. Based upon data available from 96.9 percent of patients (n=10,611) who were followed for 165 days or longer, endpoint events were reduced from 13.6 percent with placebo to 12.1 percent with eptifibatide 180/2.0 (p=0.021 log rank) at the six-month timepoint.

In our August 9, 1999 approvable letter for this supplement, we indicated that this supplement was approvable, provided you submit final printed labeling revised as follows:

> The paragraph added to the **CLINICAL STUDIES** section, immediately preceding the IMPACT II study description, was replaced with the following paragraph:
>
> > Follow-up data were available through 165 days for 10,611 patients enrolled in the PURSUIT trial (96.9 percent of the initial enrollment). This follow-up included 4566 patients who received eptifibatide at the 180/2.0 dose. As reported by the investigators, the occurrence of death from any cause or new myocardial infarction for patients followed for at least 165 days was reduced from 13.6 percent with placebo to 12.1 percent with eptifibatide 180/2.0.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the final printed labeling included in your August 20, 1999 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

We note your commitment, as agreed to by Ms. Arleen Glenn, Associate Director of Regulatory Affairs, COR Therapeutics, Inc., in a September 3, 1999 telephone conversation with Ms. Colleen LoCicero, Regulatory Health Project Coordinator, Division of Cardio-Renal Drug Products, to amend the labeling, at your next printing, to present the serum creatinine values consistently throughout the package insert (i.e., express the values as either all whole numbers or all decimal numbers), and to report this change in your next annual report.

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:

Ms. Colleen LoCicero
Regulatory Health Project Coordinator
(301) 594-5334

Sincerely yours,

Ray Lipicky

Raymond J. Lipicky, M.D.
Director
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