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APPROVAL PACKAGE FOR:

APPLICATION NUMBER
20-718/S-010

Approval Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-718/S-010
S-013

JUN 8 2001

COR Therapeutics, Inc.
Attention: Michael R. Marsman, Pharm.D.
256 East Grand Avenue
South San Francisco, CA 94080

Dear Dr. Marsman:

Please refer to your supplemental new drug applications dated June 29, 2000 (S-010) and February 12, 2001 (S-013), received June 30, 2000 and February 13, 2001, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Integrilin (eptifibatide) Injection.

We acknowledge receipt of your submission dated May 14, 2001 that constituted a complete response to our March 28, and April 30, 2001 action letters.

S-010 provides for labeling revised to reflect the findings of the ESPRIT ("Enhanced Suppression of the Platelet IIb/IIIa Receptor with Integrilin Therapy (the 'ESPRIT Study); A Phase III Study in Patients Undergoing Percutaneous Coronary Intervention with Stent Implantation") study. The revisions include a new dosing recommendation for patients undergoing Percutaneous Coronary Intervention (PCI) and a revised recommended target range for the activated clotting time (ACT) during PCI.

S-013 provides for the addition of information to the package insert on bleeding events from post-marketing adverse event reports.

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 product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted May 14, 2001). Accordingly, these supplemental applications are approved effective on the date of this letter.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). As stated in our August 28, 2000 response to your August 4, 2000 request for a waiver of the pediatric study requirement for this application, we have waived the pediatric study requirement for this application.

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 yours, 6/8/01

{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

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NDA 20-718/S-010

APR 30 2001

COR Therapeutics, Inc.
Attention: Michael R. Marsman, Pharm.D.
256 East Grand Avenue
South San Francisco, CA 94080

Dear Dr. Marsman:

Please refer to your supplemental new drug application dated June 29, 2000, received June 30, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Integrilin (eptifibatide) Injection.

We acknowledge receipt of your submissions dated August 4 and 7, 2000 and February 8, and March 9 and 14, 2001.

This supplemental new drug application proposes the following changes to the labeling:

1. The addition of a new "front loaded" dosing regimen for patients undergoing percutaneous coronary intervention (PCI).

2. The elimination of the IMPACT (Integrilin to Minimize Platelet Aggregation and Prevent Coronary Thrombosis) II study dosing recommendation for use in PCI.

3. A change in the recommended target range for the activated clotting time (ACT) during PCI.

4. The movement of information regarding renal insufficiency and thrombocytopenia from the **CONTRAINDICATIONS** section to the **WARNINGS** section of the package insert.

5. Additional changes throughout the package insert to reflect the ESPRIT findings.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the enclosed labeling (text for the package insert).

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

Please submit the copies of final printed labeling (FPL) electronically 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, ten of which individually mounted on heavy weight paper or similar material.

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

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the supplemental application, 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 application. 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.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, please call:

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

Sincerely yours,

{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

Enclosure

50 pages redacted from this section of the approval package consisted of draft labeling

(1-50)