CENTER FOR DRUG EVALUATION AND RESEARCH

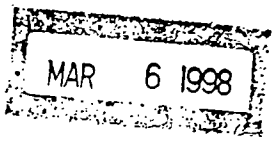
Application Number: 020807

APPROVAL LETTER

Letter

NDA 20-807

Hoechst Marion Roussel
C/O ClinTrials Research, Inc. (U.S. Agent)
Attention: B. Randall Vestal
P.O. Box 13991
Research Triangle Park, North Carolina 27709



Dear Mr. Vestal:

Please refer to your new drug application dated December 31, 1996, received December 31, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Refludan® [lepirudin (rDNA) for Injection].

We acknowledge receipt of your submissions dated September 16, October 2, November 21 and 26, December 1, 8, and 11, 1997, and February 23, 1998. The User Fee goal date for this application is May 24, 1998.

This new drug application provides for the use of Refludan® [lepirudin (rDNA) for Injection] for anticoagulation in patients with heparin-induced thrombocytopenia (HIT) and thromboembolic disease in order to prevent further thromboembolic complications.

We have completed the review of this application, including the submitted draft labeling, 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 enclosed draft labeling. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed draft labeling. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case 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, this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-807. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

In addition, please submit three copies of the introductory promotional material 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 the Division of Gastrointestinal and Coagulation Drug Products and two copies of both the promotional material and the package

BEST POSSIBLE COPY

insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications, HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug product when it is available.

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 Julieann DuBeau, Regulatory Health Project Manager, at (301) 443-0487.

Sincerely yours,

/S/ 3/6/98

APPEARS THIS WAY
ON ORIGINAL

Paula Botstein, M.D.
Acting Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE

APPEARS THIS WAY
ON ORIGINAL

cc:
Original NDA 20-807
HFD-180/Div. files
HFD-180/CSO/J.DuBeau /S/ 2-25-98
HFD-180/Talarico
HFD-002/ORM (with labeling)
HFD-103/Office Director
HFD-101/L.Carter

HFD-820/ONDC Division Director
DISTRICT OFFICE
HF-2/Medwatch (with labeling)
HFD-92/DDM-DIAB (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-735/DPE (with labeling) - for all NDAs and supplements for adverse reaction changes.
HFI-20/Press Office (with labeling)
r/d Init: Johnson 2/27/98
JD/February 27, 1998 (drafted)
JD/2/27/98/c:\wpfiles\nda\20807802.1jd

APPEARS THIS WAY
ON ORIGINAL

/S/ 2/27/98

APPROVAL (AP)

APPEARS THIS WAY
ON ORIGINAL

FINAL PRINTED LABELING HAS NOT BEEN SUBMITTED TO THE FDA.

DRAFT LABELING IS NO LONGER BEING SUPPLIED SO AS TO ENSURE ONLY CORRECT AND CURRENT INFORMATION IS DISSEMINATED TO THE PUBLIC.