021546_ Original_ Approval_ RKG.

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number 21-546

Trade Name Rebetol

Generic Name ribavirin

Sponsor Schering Corp.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION 21-546

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Application Number 21-546

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

Food and Drug Administration
Rockville MD 20857

NDA 21-546

Schering Corporation
Attention: Isidoro J. Perez
Vice President, U.S. Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Mr. Perez,

Please refer to your new drug application (NDA) dated January 29, 2003, received January 30, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for REBETOL® (ribavirin, USP) Oral Solution.

We acknowledge receipt of your submissions dated April 11, 2003, April 22, 2003, June 27, 2003, June 30, 2003, July 14, 2003, July 21, 2003, July 25, 2003, and July 29, 2003.

This new drug application provides for the use of REBETOL® (ribavirin, USP) Oral Solution to be used as part of combination therapy with INTRON A® for the treatment of chronic hepatitis C among previously untreated pediatric patients at least three years of age or older.

We have completed the review of this 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 agreed upon labeling text. Accordingly, this application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the Medication Guide, immediate container and carton labels) and/or submitted labeling (package insert submitted July 25, 2003, Medication Guide submitted July 25, 2003, immediate container and carton labels submitted June 30, 2003), and must be in the "Drug Facts" format (21 CFR 201.66). Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and (an) unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-546.**" Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitment in your submission dated July 29, 2003. This commitment is listed below:

1. **Long-Term Follow-Up:** Patients who completed 24 weeks of follow-up in Protocols P00018 or P00321 are eligible to enroll in Protocol P01906, "Long-Term Follow-Up Protocol to Assess Pediatric Subjects After Completing 24 Weeks of Follow-Up in a SPRI Clinical Trial for the Treatment of Chronic Hepatitis C." This protocol was amended to ——— on March 20, 2001 (Serial No.: 397) and enrollment began in July 2001. Patients will be evaluated yearly for 5 years beginning 12 months after the last visit (ie., follow-up week 24) on study P00018 or P00321.

   Final Report Submission: December 2008

In addition, submit three copies of the introductory promotional materials that you propose to use for this/these product(s). Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this the Division of Antiviral Drug Products and two copies of both the promotional materials and the package insert(s) directly to:

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

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

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, please call Destry Sillivan, Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Debra Birnkrant
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NDA 21-546

APPEARS THIS WAY
ON ORIGINAL