020903_s008$s011
$s012$5016

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package

APPLICATION NUMBER:

20-903/S-008, S-011, S-012, S-016

Trade Name: Rebetol® / Rebetron Combination Therapy™

Generic Name: (ribavirin / ribavirin and Intron® A)

Sponsor: Schering Corporation

Approval Date: July 25, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-903/S-008, S-011, S-012, S-016

CONTENTS

Reviews / Information Included in this NDA Review.	
Approval Letter	X
Approvable Letter	
Final Printed Labeling	X
Medical Review(s)	X
Chemistry Review(s)	
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative and Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-903/S-008, S-011, S-012, S-016

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-903/S-008, S-011, S-012, S-016

Schering Corporation
Attention: Joseph F. Lamendola
Senior Director, Marketed Products, Support and Training
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Dr. Lamendola,

Please refer to your supplemental new drug applications dated November 7, 2000, February 26, 2001, February 28, 2001, and May 11, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for REBETOL® (ribavirin) capsules for use in combination with the approved biologic product Intron®A (interferon alfa 2b) (Rebetron Combination Therapy™).

We acknowledge receipt of your submissions for supplemental new drug application S-008 dated November 7, 2000, January 5, 2001, May 3, 2001, May 16, 2001, June 1, 2001, July 20, 2001, and July 25, 2001.

We also acknowledge receipt of your submissions for supplemental new drug application S-011 dated February 26, 2001, March 7, 2001, May 17, 2001, July 20, 2001, and July 25, 2001.

In addition, we acknowledge receipt of your submissions for supplemental new drug application S-012 dated February 28, 2001, March 6, 2001, May 14, 2001, July 20, 2001, and July 25, 2001.

Finally, we acknowledge receipt of your submissions for supplemental new drug application S-016 dated May 11, 2001, May 18, 2001, July 20, 2001, and July 25, 2001.

The supplemental new drug application S-008 provides for the marketing of a separate 84 capsule container of REBETOL® (ribavirin) capsules for use in combination with the approved biologic product Intron®A (interferon alfa 2b) (Rebetron Combination Therapy™) for adult patients with chronic hepatitis C virus (HCV) infection.

The supplemental new drug application S-011 provides for revisions to the Medication Guide for Rebetron Combination Therapy™ to provide information to patients on how to utilize the multidose pen injector to avoid discoloration observed in post-marketing reports for Rebetron Combination Therapy™.

The supplemental new drug application S-012 provides for the implementation of a "Safety-Lok Syringe" to replace the syringe previously marketed with Rebetron Combination Therapy™.

The supplemental new drug application S-016 provides for the inclusion of an official Medication Guide for REBETOL® (ribavirin) capsules and for Rebetron Combination Therapy™[REBETOL® (ribavirin) capsules, Intron®A (interferon alfa 2b)], pursuant to 21 CFR Part 208. d

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 agreed upon enclosed labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the Final Draft Labeling submitted July 25, 2001 (text for the package insert, text for the patient package insert, immediate container and carton labels).

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 as soon as it is available but no 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 "FPL for approved supplements NDA 20-903/S-008, S-011, S-012, S-016." Approval of this submission by FDA is not required before the labeling is used.

Pursuant to 21 CFR Part 208, FDA is notifying you that you are required to distribute a Medication Guide for REBETOL® (ribavirin) capsules and Rebetron Combination Therapy™. The FDA has determined that REBETOL® (ribavirin) capsules and Rebetron Combination Therapy™ pose a serious and significant public health concern, and therefore, requires the distribution of a Medication Guide. Distribution of a Medication Guide is necessary for the safe and effective patient use of REBETOL® (ribavirin) capsules and Rebetron Combination Therapy.

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

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

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, call Destry M. Sillivan, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Acting 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
7/25/01 03:51:15 PM
NDA 20-903, SLR 008, 011, 012, 016