DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-903/S-040

Schering Corporation
Attention: Rachael Steiner
Associate Director and Liaison
Global Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Ms. Steiner:

Please refer to your supplemental new drug application dated June 1, 1007, received on June 4, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for REBETOL® (Ribavirin, USP), Capsules, 200 mg and Oral Solution 40 mg/mL.

We acknowledge receipt of your submissions dated November 28, 2007 and December 3, 2007.

This supplemental new drug application was submitted to revise the PRECAUTIONS-Animal Toxicology subsection of the package insert based on the findings of a series of three oral toxicity studies that were conducted in neonatal rats to assess the reproductive and development toxicity of ribavirin, and the DOSAGE and ADMINSTRATION section of the package insert to include the statement "under no circumstances should the capsules be opened, crushed or broken," and to add this statement to the "How Should I take Rebetol Capsules or Oral Solution" section of the Medication Guide.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 20-903."

The final printed labeling (FPL) must be identical to the package insert submitted on November 28, 2007 and the Medication Guide submitted on December 3, 2007.

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

If you have any questions, call Victoria Tyson-Medlock, Regulatory Project Manager, at (301) 796-0827.

Sincerely,

{See appended electronic signature page}

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

Enclosure (package insert and Medication Guide)

112807.final draft PI -F-XXXXXXXX

PRODUCT INFORMATION

REBETOL® (ribavirin, USP) Capsules and Oral Solution

- REBETOL MONOTHERAPY IS NOT EFFECTIVE FOR THE TREATMENT OF CHRONIC HEPATITIS C VIRUS INFECTION AND SHOULD NOT BE USED ALONE FOR THIS INDICATION. (SEE WARNINGS.)
- THE PRIMARY TOXICITY OF RIBAVIRIN IS HEMOLYTIC ANEMIA. THE ANEMIA ASSOCIATED WITH REBETOL THERAPY MAY RESULT IN WORSENING OF CARDIAC DISEASE THAT HAS LED TO FATAL AND NONFATAL MYOCARDIAL INFARCTIONS. PATIENTS WITH A HISTORY OF SIGNIFICANT OR UNSTABLE CARDIAC DISEASE SHOULD NOT BE TREATED WITH REBETOL. (SEE WARNINGS, ADVERSE REACTIONS, AND DOSAGE AND ADMINISTRATION.**)**
- SIGNIFICANT TERATOGENIC AND/OR EMBRYOCIDAL EFFECTS HAVE BEEN DEMONSTRATED IN ALL ANIMAL SPECIES EXPOSED TO RIBAVIRIN. IN ADDITION, RIBAVIRIN HAS A MULTIPLE-DOSE HALF-LIFE OF 12 DAYS, AND SO IT MAY PERSIST IN NONPLASMA COMPARTMENTS FOR AS LONG AS 6 MONTHS. THEREFORE, REBETOL THERAPY IS CONTRAINDICATED IN WOMEN WHO ARE PREGNANT AND IN THE MALE PARTNERS OF WOMEN WHO ARE PREGNANT. EXTREME CARE MUST BE TAKEN TO AVOID PREGNANCY DURING THERAPY AND FOR 6 MONTHS AFTER COMPLETION OF TREATMENT IN BOTH FEMALE PATIENTS AND IN FEMALE PARTNERS OF MALE PATIENTS WHO ARE TAKING REBETOL THERAPY. AT LEAST TWO RELIABLE FORMS OF EFFECTIVE CONTRACEPTION MUST BE UTILIZED DURING TREATMENT AND DURING THE 6-MONTH POSTTREATMENT FOLLOW-UP PERIOD. (SEE CONTRAINDICATIONS, WARNINGS, PRECAUTIONS-INFORMATION FOR PATIENTS AND PREGNANCY CATEGORY X.)

DESCRIPTION

REBETOL®

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
12/4/2007 04:04:14 PM
NDA 20-903