DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20-903/S-046
NDA 21-546/S-002

SUPPLEMENT APPROVAL

Schering Corporation
Attention: Ripal Shah, Pharm D.
Manager, Global Regulatory Affairs
2000 Galloping Hill Rd.
Kenilworth, NJ 07033

Dear Dr. Shah:

Please refer to your Supplemental New Drug Applications (sNDAs) dated November 24, 2009, received November 27, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for REBETOL® (ribavirin) 200 mg Capsules and 40 mg per mL Oral Solution.

We acknowledge receipt of your amendments dated July 30, 2010, September 22, 2010 and October 6, 2010; and your risk evaluation and mitigation strategy (REMS) assessment dated November 24, 2009.

These "Prior Approval" supplemental new drug applications update the Warnings and Precautions and Drug Interactions sections of the Prescribing Information to include information on cases of pancytopenia and bone marrow suppression with concomitant use of azathioprine and pegylated interferon/ribavirin, and corresponding changes to the "What is the most important information I should know about REBETOL?", "What should I tell my healthcare provider before taking REBETOL?" and the "What are the possible side effects of REBETOL?" sections of the Medication Guide and other changes to the Medication Guide based on the review of the REMS assessment submitted on November 24, 2009.

We have completed our review of these supplemental applications, as amended. These supplements are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry

titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for REBETOL® (ribavirin) was originally approved on November 6, 2009. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of a revised Medication Guide with updates to the "What should I tell my healthcare provider before taking REBETOL?" and the "What are the possible side effects of REBETOL?" sections of the Medication Guide and other changes based on our review of your REMS assessment submitted on November 24, 2009.

Your proposed modified REMS, submitted on July 30, 2010 and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on November 6, 2009.

There are no changes to the REMS assessment plan described in our November 6, 2009, letter.

Assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to

the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you will also need to submit a REMS, REMS supporting document, and any required appended documents for that authorized generic, to this NDA. In other words, you must submit a complete proposed REMS that relates only to the authorized generic product. Review and approval of the REMS is required before you may market your product.

Prominently identify the submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 20-903 REMS ASSESSMENT
NDA 21-546 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 20-903 or NDA 21-546
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 20-903 or NDA 21-546
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

REPORTING REQUIREMENTS

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, 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

ENCLOSURES:
Content of Labeling
REMS

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

/s/

VENESSA M PERRY
10/28/2010

KENDALL A MARCUS
10/28/2010