



NDA 22081/S-016

SUPPLEMENT APPROVAL

Gilead Sciences, Inc.
Attention: Ellen L. Shen, Ph.D.
Associate Manager, Regulatory Affairs
333 Lakeside Dr.
Foster City, CA 94404

Dear Dr. Shen:

Please refer to your supplemental New Drug Application (sNDA) dated April 8, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Letairis (ambrisentan) 5 and 10 mg Tablets.

We also acknowledge receipt of your amendments dated June 10, 15, and July 21, 2010, and your risk evaluation and mitigation strategy (REMS) assessment dated April 8, 2010.

This Prior Approval sNDA provides for a proposed modification to the approved REMS and revisions to the REMS supporting document.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Letairis was originally approved on May 29, 2009, and a REMS modification was approved on August 5, 2009. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of a revised timetable for submission of assessments as follows:

FROM

Following approval of the REMS, the REMS assessments will be submitted to the FDA annually. The assessment interval period will close no earlier than 60 days prior to the date the respective assessment is due. The assessment is to be received by the FDA on the due date.

TO

Gilead will submit REMS assessments to the FDA annually on August 13th. The assessment interval period will close no earlier than 60 days prior to the date the

respective assessment is due. The assessment is to be received by the FDA on the due date.

Your proposed modified REMS, submitted on June 15, 2010 and appended to this letter, is approved. We also find the proposed revisions to the REMS supporting document to be acceptable.

There are no changes to the REMS assessment plan described in our May 29, 2009 letter.

We remind you that the requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(A), an assessment of the extent to which the elements to assure safe use are meeting the goal or goals to mitigate a specific serious risk listed in the labeling of the drug, or whether the goal or goals or such elements should be modified.

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.

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.

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

**NDA 22081
REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 22081-PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATION
REMS ASSESSMENT**

NEW SUPPLEMENT (NEW INDICATION FOR USE)

**FOR NDA 22081
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

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, please call Dan Brum, PharmD, RAC, Regulatory Project Manager, at (301)796-0578.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director of Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Modified REMS

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22081

SUPPL-16

GILEAD SCIENCES
INC

LETAIRIS

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

/s/

MARY R SOUTHWORTH

08/24/2010