DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204819/S-001

SUPPLEMENT APPROVAL

Bayer Healthcare Pharmaceuticals Inc.
Attention: Sharon Brown
Director, Global Regulatory Affairs
100 Bayer Blvd
P.O. Box 915
Whippany, NJ 07981-0915

Dear Ms. Brown:

Please refer to your Supplemental New Drug Application (sNDA) dated December 10, 2013 and received December 11, 2014, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Adempas (riociguat) 0.5 mg, 1 mg, 1.5 mg, 2 mg, and 2.5 mg Tablets.

We also refer to your amendments dated February 6, March 24, and April 16, 2014.

This Prior Approval supplement provides for modifications to the approved Adempas risk evaluation and mitigation strategy (REMS).

We have completed our review of this supplemental application, as amended, and it is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Adempas (riociguat) was originally approved on October 8, 2013. 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 modifications to the REMS consist of:

- An update to the REMS website to include links to Spanish versions of the Medication Guide and the REMS Guide for Females Who Can Get Pregnant.
- A logo change to add tablet dose availability just below the words “Adempas” and “riociguat tablets”.
- An update to the REMS website so that when one clicks on the Patient Information Tab, the important safety information (ISI) for the patient appears.
- Administrative changes to the Veteran’s Administration (VA) Adempas Patient Enrollment and Consent Form.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Your proposed modified REMS, submitted on December 11, 2013, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on October 8, 2013.

There are no changes to the REMS assessment plan described in our October 8, 2013, letter.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 204819 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission 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 204819 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 204819
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 204819
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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

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, please call:

Lori Anne Wachter, RN, BSN
Regulatory Project Manager for Safety
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

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
06/11/2014