



NDA 204819/S-007

**SUPPLEMENT APPROVAL**

Bayer HealthCare Pharmaceuticals, Inc.  
Attention: Joseph Quintavalla, PhD  
Deputy Director, Regulatory Affairs  
100 Bayer Boulevard  
P.O. Box 915  
Whippany, NJ 07981-0915

Dear Dr. Quintavalla:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 5, 2016, and your amendments dated September 28, 2016, submitted under section 505(b) 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.

This supplemental new drug application provides for proposed modifications to the approved risk evaluation and mitigation strategy (REMS) for Adempas (riociguat).

**RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for Adempas (riociguat) was originally approved on October 8, 2013, and the most recent modification was approved on December 4, 2015. 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:

- Removal of non-REMS related information from *the Adempas REMS Patient Enrollment and Consent Form*
- Elimination of the *VA REMS Patient Enrollment and Consent Form*
- Addition of the word "REMS" to the title of the following forms: *Adempas REMS Patient Enrollment and Consent Form* and *Adempas REMS Patient Enrollment and Consent Form*

Your proposed modified REMS, submitted on August 5, 2016, and appended to this letter, is approved.

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

There are no changes to the REMS assessment plan described in our December 4, 2015 letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that 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 the FDCA. This assessment should include:

- a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
- b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
- c) *If the new indication for use introduces unexpected risks:* A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
- d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* A statement about whether the REMS was meeting its goals at the time of the last assessment and if any modifications of the REMS have been proposed since that assessment.
- e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
- f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications, provide a rationale for why the REMS does not need to be modified.*

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.

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.



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

Sincerely,

*{See appended electronic signature page}*

Mary Ross Southworth, PharmD.  
Deputy Director for Safety  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
REMS

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MARY R SOUTHWORTH  
10/04/2016