NDA 204819/S-019

SUPPLEMENT APPROVAL

Bayer HealthCare Pharmaceuticals Inc.
Attention: Kay Owosela, MSc, RAC
Director, US Regulatory Liaison
100 Bayer Boulevard
P.O. Box 0915
Whippany, NJ 07981

Dear Kay Owosela:

Please refer to your supplemental new drug application (sNDA) dated and received February 20, 2026, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Adempas (riociguat) tablets.

This Prior Approval supplemental new drug application provides for labeling changes to update content related to embryo fetal toxicity and proposed modifications to the approved Riociguat Shared System (SS) risk evaluation and mitigation strategy (REMS).

APPROVAL & LABELING

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling with minor editorial revisions listed below and reflected in the enclosed labeling (insertions are shown as underlined text and deletions are shown in ~~strikethrough text~~:

- In the Medication Guide under the question What is most important information I should know about Adempas?, the following text was revised:

  Adempas ~~can~~may cause serious birth defects if taken during pregnancy.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including 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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The SS REMS for Riociguat products, of which Adempas is a member, was originally approved on September 1, 2022, and the most recent REMS modification was approved on May 8, 2026. The SS REMS consists of 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 eliminating the Riociguat SS REMS

Elements to Assure Safe Use: We have determined that elements to assure safe use are no longer necessary to ensure the benefits of Adempas outweigh its risks because our evaluation of human fetal outcomes reported from 2013 to 2026 after exposure to riociguat has not identified any major cardiac malformations consistent with what was observed in the animal embryo-fetal toxicity studies that supported the need for a REMS. Given the re-evaluation of the extent of the clinical risk finds it is limited to animal findings and the recognition that embryo-fetal risk mitigation is reinforced through routine clinical management of the underlying disease, we have determined that labeling is sufficient for conveying information about the embryo-fetal risk and its mitigation.

Implementation System: In addition, because the elements to assure safe use requiring that pharmacies, practitioners, or health care settings that dispense the drug

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

be specially certified and the drug be dispensed to patients with documentation of safe use conditions are no longer necessary, the implementation system is also no longer necessary as an element of the REMS.

Therefore, because the elements to assure safe use and the implementation system are no longer necessary to ensure the benefits of the drug outweigh the risks, a REMS is no longer required for riociguat.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[3] Information and Instructions for completing the form can be found at FDA.gov.[4]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety- related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

[3] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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, contact Lori Anne Wachter, RN, BSN, RAC – Drugs (US), Regulatory Project Manager for Safety, at 301 796-3975 or lori.wachter@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Selena DeConti, PharmD, MPH
Deputy Director for Safety
Division of Cardiology and Nephrology
Office of Cardiology, Hematology, Endocrinology and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SELENA D DECONTI
08/04/2026 10:13:00 AM