Important Safety Information on ADEMPAS® (riociguat) - New contraindication for patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP)

15/08/2016

Audience
Healthcare professionals who prescribe ADEMPAS (riociguat) and hospital clinics managing patients with Pulmonary Hypertension

Key messages

- **Patients with PH-IIP should not be treated with ADEMPAS. If any patients with PH-IIP are being treated with ADEMPAS, their treatment should be discontinued and their clinical status carefully monitored.**
- **The RISE-IIP study, which was investigating the effects of ADEMPAS in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP), has been terminated early due to an increased risk of mortality and serious adverse events among subjects with PH-IIP receiving ADEMPAS.**
- **The Canadian Product Monograph will be updated to reflect the contraindication for ADEMPAS in PH-IIP.**

What is the issue?
The RISE-IIP study, which was evaluating efficacy and safety of ADEMPAS (riociguat) in patients with symptomatic PH-IIP, has been terminated early, because interim results of RISE-IIP showed an increased risk of mortality and serious adverse events among patients receiving ADEMPAS compared to those receiving placebo. The available data indicate that the use of ADEMPAS in patients with PH-IIP presents greater risks than benefits.

Products affected
ADEMPAS (riociguat tablets), manufactured by Bayer Inc.

Background information
ADEMPAS is not authorized for the treatment of PH-IIP.
It is indicated in adult patients for the treatment of:

- inoperable chronic thromboembolic pulmonary hypertension
- persistent or recurrent chronic thromboembolic pulmonary hypertension after surgical treatment
- pulmonary arterial hypertension, as monotherapy or in combination with endothelin receptor antagonists

The RISE-IIP study was a randomized, double-blind, placebo-controlled, multicentre phase II clinical trial to investigate the efficacy and safety of ADEMPAS in patients with symptomatic PH-IIP.

The RISE-IIP study was recently terminated early on the recommendation of the Data Monitoring Committee. An evaluation of the interim results by the Sponsor and Health Canada concluded that the benefit-risk balance of ADEMPAS in patients with PH-IIP is negative. The ADEMPAS Canadian Product Monograph will be updated to contraindicate the use of ADEMPAS in patients with PH-IIP.

Information for consumers

A clinical trial studying ADEMPAS in patients with PH-IIP was stopped early because more serious problems or deaths were seen in patients taking ADEMPAS than in patients taking placebo. PH-IIP is a rare condition where there is high blood pressure in the arteries of the lungs caused by a lung disease called idiopathic interstitial pneumonia (IIP).

ADEMPAS should not be used to treat PH-IIP. If any patients are taking ADEMPAS for PH-IIP, they should contact their physician immediately about managing their disease.

ADEMPAS remains an authorized treatment for adults with the following forms of pulmonary hypertension (high blood pressure in the lungs), as the benefit of ADEMPAS for these uses outweigh the risks:

- Chronic thromboembolic pulmonary hypertension (where the blood vessels of the lungs are blocked or narrowed with blood clots).
- Pulmonary arterial hypertension (where the walls of the blood vessels of the lungs are thickened and the vessels become narrowed).

Information for health care professionals

A contraindication in PH-IIP patients will be added to the Canadian Product Monograph for ADEMPAS following the early termination of the RISE-IIP clinical trial and based on preliminary data from the trial.

Health care professionals should not prescribe ADEMPAS for patients with PH-IIP. If any patients with PH-IIP are being treated with ADEMPAS their treatment should be discontinued and their clinical status carefully monitored.

The benefit-risk profile of ADEMPAS in its approved indications (inoperable and recurrent/persistent Chronic Thromboembolic Pulmonary Hypertension and Pulmonary Arterial Hypertension) remains favourable.

Action taken by Health Canada

Health Canada is working with the manufacturer to update the Canadian Product Monograph with a contraindication in patients with PH-IIP.

Health Canada will continue to monitor safety information associated with the use of ADEMPAS and will take action as appropriate if any new safety information is identified.

Report health or safety concerns

Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Any suspected adverse reactions in patients receiving ADEMPAS should be reported to Bayer Inc. or Health Canada.

Bayer Inc.
2920 Matheson Boulevard East
Mississauga, ON
L4W 5R6
Telephone: 1-800-265-7382
Email: canada.medinfo@bayer.com

To correct your mailing address or fax number, contact Bayer Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate (MHPD)
E-mail: mhpd_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

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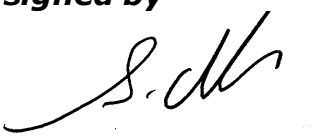

Shurjeel Choudhri, MD, FRCPC
Senior Vice President & Head, Medical and Scientific Affairs
Bayer Inc.