4th July 2016

Riociguat (Adempas®): New contraindication in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP)

Dear Healthcare Professional,

Bayer Pharma AG and MSD in agreement with the European Medicines Agency and the Health Products Regulatory Authority would like to inform you of the following:

Summary

- Patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP) should not be treated with riociguat.
- The RISE-IIP study, which evaluated efficacy and safety of riociguat in patients with symptomatic PH-IIP has been terminated early. Riociguat is not authorised for this indication.
- Interim results of RISE-IIP showed an increased risk of mortality and serious adverse events among subjects receiving riociguat compared to those receiving placebo. The available data do not indicate a clinically significant benefit in these patients.
- If any patients with PH-IIP are being treated with riociguat their treatment should be discontinued and their clinical status carefully monitored.
- The benefit-risk profile of Adempas in its approved indications remains positive.

Further information on the safety concerns and the recommendation

The RISE-IIP study was a randomised, double-blind, placebo-controlled, multicentre phase II study to investigate the efficacy and safety of riociguat in patients with symptomatic pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP).

Riociguat is not authorised for the treatment of pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP). RISE-IIP was recently terminated early on the recommendation of the Data Monitoring Committee (DMC). An evaluation of the interim results by the EMA concluded that the benefit risk balance of riociguat in patients with PH-IIP is negative. The information for healthcare professionals in the Adempas Summary of Product Characteristics (SmPC) and the information for patients in the package leaflet will be updated to contraindicate the use of riociguat in patients with PH-IIP.

Adempas is approved for use in patients with WHO Functional Class (FC) II-III inoperable chronic thromboembolic pulmonary hypertension (CTEPH) or persistent or recurrent CTEPH after surgery, and in patients with WHO FC II-III pulmonary arterial hypertension (PAH).

In pulmonary arterial hypertension, studies with riociguat have been mainly performed in forms related to idiopathic or heritable PAH and PAH associated with connective tissue disease. The use of riociguat in other forms of PAH that have not been studied is not recommended.

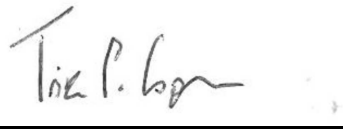
The benefit-risk profile of Adempas in its approved indications remains positive.

Reporting adverse drug reactions

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via: HPRA Pharmacovigilance, Earlsfort Terrace, IRL-Dublin 2; Tel: +3531 6764971; Fax: +3531 6762517. Website: www.hpra.ie. Adverse events should also be reported to MSD Ireland (Human Health) at +353 (0)1 299 8700.

If you have any questions, or if you require any further information, please contact the medical information service of MSD Ireland (Human Health) at +353 (0)1 299 8700 or medinfo_ireland@merck.com.

With kind regards,



Dr. Tristan P Cooper
Medical Director
Bayer Ltd.

Dr. Colm Galligan
Medical Director
MSD