Drug Safety Update

Latest advice for medicines users

The monthly newsletter from the Medicines and Healthcare products Regulatory Agency and its independent advisor the Commission on Human Medicines

Volume 10, Issue 1, **August 2016**

Contents

The Medicines and Healthcare products Regulatory Agency is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

NICE accredited
www.nice.org.uk/accreditation

The MHRA is accredited by NICE to provide Drug Safety Update. Further information can be found on the NICE Evidence Search portal: www.evidence.nhs.uk/

Patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP) should not be treated with riociguat in light of interim results from a recently terminated study called RISE-IIP. The trial was investigating the efficacy and safety of riociguat in patients with symptomatic pulmonary hypertension associated with PH-IIP—an unapproved indication. The trial was terminated early on the basis of interim results that showed increased mortality and increased risk of serious adverse events in the riociguat group compared with the placebo group, in the absence of clinically significant benefit.

Riociguat treatment should be discontinued in any patient with PH-IIP, and the patient's clinical status should be carefully monitored after stopping. The benefits of riociguat in its approved indications continue to outweigh the risks. These indications are: WHO Functional Class II–III inoperable chronic thromboembolic pulmonary hypertension (CTEPH), or persistent or recurrent CTEPH after surgery; and WHO Functional Class II–III pulmonary arterial hypertension. Further information about the interim trial results is on page 2.

drugsafetyupdate@mhra.gsi.gov.uk

Riociguat (Adempas): not for use in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias

Patients with pulmonary hypertension associated with idiopathic interstitial pneumonias should not be treated with riociguat in light of interim results from a recently terminated study.

Advice for healthcare professionals:

- patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP) should not be treated with riociguat. PH-IIP is not authorised indication for riociguat
- riociguat treatment should be discontinued in any patient with PH-IIP. The patient's clinical status should be carefully monitored after stopping riociguat
- the benefits of riociguat in its approved indications (see below) continue to outweigh the risks

Indications

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

RISE-IIP trial

RISE-IIP was a randomised, double-blind, placebo-controlled, multicentre phase II trial to investigate the efficacy and safety of riociguat in 145 patients with symptomatic PH-IIP—an unapproved indication. The primary endpoint was change in the 6-minute walking-distance test after 26 weeks of treatment.

Early termination of trial

The trial was terminated early on the basis of interim results that showed increased mortality and increased risk of serious adverse events in the riociguat group compared with the placebo group.

Moreover, preliminary data indicated that riociguat did not provide a clinically significant benefit for these patients.

At the time of the interim assessment leading to termination of the trial, 21 deaths had been observed: 17 patients assigned riociguat and 4 assigned placebo. Serious adverse events, which were mainly respiratory disease or lung infections, were also higher in the riociguat group than in the placebo group.

In light of these findings, product information for riociguat will be updated to contraindicate the use of riociguat in patients with PH-IIP. The benefits of riociguat in its approved indications continue to outweigh the risks.

Continues…

PAH

Studies of riociguat in patients with PAH have mainly assessed forms related to idiopathic PAH, heritable PAH, and that associated with connective-tissue disease. Use of riociguat in other forms of PAH that have not been studied is not recommended (further information is given in sections 4.4 and 5.1 of the Summary of Product Characteristics).

Further information

Letter sent to healthcare professionals, 4 July 2016

European Medicines Agency statement for riociguat, 24 June 2016

Article citation: Drug Safety Update volume 10 issue 1 August 2016: 1

Letters sent to healthcare professionals in July 2016

In July 2016, the following letters were sent to relevant healthcare professionals:

- riociguat (Adempas): not for use in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias (see also article above)
- posaconazole (Noxafil): tablets and oral suspension are not interchangeable

Article citation: Drug Safety Update volume 10 issue 1 August 2016: 2.