EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Media and Public Relations

News announcement

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 26 – 29 September

Codeine with ibuprofen: PRAC adds warning for serious renal and gastrointestinal harms

The PRAC has recommended a change to the product information for codeine with ibuprofen combination medicines to include a warning of serious harms, including death, particularly when taken for prolonged periods at higher than recommended doses.

Codeine with ibuprofen is a combination of two medicines, an opioid (codeine) and an anti-inflammatory (ibuprofen), which are used to treat pain. Repeated use of codeine/ibuprofen may lead to dependence (addiction) and abuse due to the codeine component.

The committee reviewed several cases of renal, gastrointestinal and metabolic toxicities that have been reported in association with cases of abuse and dependence for codeine with ibuprofen combinations, some of which have been fatal.

The PRAC found that, when taken at higher than recommended doses or for a prolonged period of time, codeine with ibuprofen can cause damage to the kidneys, preventing them from removing acids properly from the blood into the urine causing a rare disease known as renal tubular acidosis. Kidney malfunction can also cause very low levels of potassium in blood (hypokalaemia) which in turn may cause symptoms such as muscle weakness and light-headedness. Renal tubular acidosis and hypokalaemia will be added to the product information as new side-effects.

As medicines containing a combination of codeine and ibuprofen are authorised at national level, the PRAC has agreed key messages that national competent authorities can use when drafting their communication to relevant healthcare professionals and to inform patients of the risks and signs of abuse and dependence from codeine with ibuprofen combinations. Patients should be advised to consult their doctor if they experience the need to use codeine with ibuprofen for more than the recommended duration and/or at higher than recommended doses.

The PRAC also noted that there are medicines containing codeine with ibuprofen which are available without medical prescription in the EU. As most of these cases were reported in countries where these medicines are available without a prescription, the PRAC considered that prescription-only medicine status would be the most effective risk minimisation measure to mitigate the harm associated with abuse and dependence of these products.

PRAC's recommendations, together with key messages for communication will be sent to the national competent authorities where a need for additional communication will be discussed at national level.

New safety information for healthcare professionals

As part of its advice on safety-related aspects to other EMA committees, the PRAC discussed a direct healthcare professional communication (DHPC) containing important information for terlipressin-containing medicines and Imbruvica.

Imbruvica (ibrutinib): new recommendations due to increased risk of cardiac events

This DHPC aims to inform healthcare professionals about an increased risk of fatal and serious cardiac arrhytmias and cardiac failure with the use of ibrutinib.

Imbruvica is a medicine for treating the blood cancers mantle cell lymphoma, chronic lymphocytic leukaemia (CLL) and Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma).

Patients with advanced age, Eastern Cooperative Oncology Group (ECOG) performance status ≥2, or cardiac co-morbidities may be at greater risk of cardiac events including sudden fatal cardiac events.
The PRAC advises that clinical evaluation of cardiac history and function should be performed before starting a treatment with ibrutinib. In patients with risk factors for cardiac events benefits and risks should be assessed before initiating treatment with the medicine and alternative treatment may be considered. Patients should be carefully monitored during treatment for signs of deterioration of cardiac function and be clinically managed.

Ibrutinib should be withheld for any new onset or worsening grade 2 cardiac failure or grade 3 cardiac arrhythmias. Treatment may be resumed as per new dose modification recommendations.

The DHPC for Imbruvica will be forwarded to EMA's human medicines committee (CHMP). Following the CHMP decision, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holder, according to an agreed communication plan, and published on the Direct healthcare professional communications page and in national registers in EU Member States.