4. October 2024

Metamizole-containing medicines: important measures to minimise the serious outcomes of known risk of agranulocytosis

Dear Healthcare professional,

<Name of marketing authorisation holder> in agreement with the <European Medicines Agency> and the <National Competent Authority> would like to inform you of the following:

Summary

- **Patients treated with metamizole-containing medicines should be informed of the:**
  - **early symptoms suggestive of agranulocytosis, including <u>fever, chills, sore throat and painful mucosal changes, especially in the mouth, nose and throat or in the genital or anal region</u>;**
  - **need to remain vigilant for these symptoms as they may occur at any time during treatment, even shortly after treatment discontinuation;**
  - **need to discontinue treatment and seek immediate medical attention if they develop these symptoms.**

- **If metamizole is taken for fever, some symptoms of emerging agranulocytosis may go unnoticed. Additionally, symptoms may also be masked in patients receiving antibiotic therapy.**

- **If agranulocytosis is suspected, a complete blood count (including differential blood count) should be performed immediately, and treatment must be stopped while waiting for the results. If confirmed, treatment must not be reintroduced.**

- **<Routine blood count monitoring of patients treated with metamizole-containing medicines is no longer recommended.>[1]**

- **Metamizole is contraindicated in patients with a prior medical history of metamizole-induced agranulocytosis (or from other pyrazolones/pyrazolidines), impaired bone marrow function or diseases of the haematopoietic system.**

Background on the safety concern

Metamizole is a pyrazolone derivative, belonging to the group of non-opioid analgesics, with potent analgesic, antipyretic and spasmolytic properties, which is indicated for the treatment of certain types of pain <and fever> as specified in the product information of each metamizole-containing medicine. Metamizole is available as a mono-component <and combination> medicinal product(s).

[1] Text in brackets to be amended at national level if routine blood count monitoring of patients treated with metamizole-containing medicines is recommended in the Product Information.

Agranulocytosis, which can lead to serious or fatal infections, is a known side effect of metamizole-containing medicines. It involves a sudden and sharp decrease in granulocyte count (neutrophil levels below $0.5x10^9$/l).

<The product information of the various metamizole-containing medicines authorised in <Member State> lists agranulocytosis with frequency rare (occurring in up to 1 in 1,000 people), very rare (occurring in up to 1 in 10,000 people) or not known (cannot be estimated from the available data).>

Following an EU-wide review, contraindications, warnings and precautions concerning the use of metamizole-containing medicines, for both patients and healthcare professionals, will be revised to minimise the serious outcomes of the known risk of agranulocytosis. This includes information when metamizole must not be used and how to facilitate prompt recognition and diagnosis of metamizole-induced agranulocytosis.

The review included an evaluation of all available data, including the scientific literature and post-marketing reports, some of which involved a fatal outcome.

The review did not identify evidence to support the effectiveness of routine blood count monitoring of patients for early recognition of the metamizole-induced agranulocytosis. Metamizole-induced agranulocytosis is not dose-dependent and can occur at any time during treatment, even in patients who have used these medicines previously without complications. Therefore, this practice is no longer recommended.

The product information of metamizole-containing medicinal products will be updated to reflect these important measures to minimise the outcomes of the risk of agranulocytosis.

Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system:

<Details (e.g., name, postal address, fax number, website address) on how to access the national spontaneous reporting system>

Company contact point

<If applicable: contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>