EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 7-10 June 2022

News 10/06/2022

EMA recommends withdrawal of marketing authorisation for amfepramone medicines

EMA's safety committee (PRAC) has recommended the withdrawal of EU marketing authorisations for amfepramone obesity medicines.

The recommendation follows a review which found that measures to restrict the use of these medicines for safety reasons have not been sufficiently effective. It found that the medicines were being used for longer than the recommended maximum period of 3 months, thereby potentially increasing the risk of serious side effects, such as pulmonary arterial hypertension (high blood pressure in the arteries of the lungs) and dependency. The medicines were also being used in patients with a history of heart disease or psychiatric disorders, increasing their risk of heart and psychiatric problems. In addition, there was evidence of use during pregnancy, which could pose risks to the unborn baby.

The review considered all available information relating to these concerns, including data from a recent EMA study on the use of these medicines in Germany and in Denmark. In addition, the PRAC received advice from a group of experts, comprising endocrinologists, cardiologists and a patient representative.

The PRAC considered introducing further measures to minimise the risk of side effects but could not identify any that would be sufficiently effective. The PRAC therefore concluded that the benefits of amfepramone medicines do not outweigh their risks and recommended that the medicines be removed from the market in the EU.

More information is available in EMA's public health communication.

Update on review of cases of heavy menstrual bleeding with mRNA COVID-19 vaccines

The PRAC is continuing its assessment of cases of heavy menstrual bleeding (heavy periods) with the COVID-19 mRNA vaccines Comirnaty and Spikevax.

Heavy periods may be defined as bleeding characterised by an increased volume and/or duration which interferes with the person's physical, social, emotional and material quality of life. Menstrual disorders are very common and can occur with a wide range of underlying medical conditions as well as from stress and tiredness. The PRAC has reviewed all the available data, including cases reported during clinical trials, cases spontaneously reported in Eudravigilance and data from the literature.

The committee agreed to continue the assessment of this safety signal and to request from the marketing authorisation holders an updated cumulative review of the cases of heavy periods.

EMA will communicate further as soon as more information is available.

PRAC finds no link between mRNA COVID-19 vaccines and absence of menstruation

The PRAC concluded that there was insufficient evidence to establish a causal association between the COVID-19 vaccines Comirnaty and Spikevax and cases of absence of menstruation (amenorrhoea).

Absence of menstruation may be defined as no bleeding for a period of 90 days or more.

The committee assessed all the available data, including findings from the literature and cases of amenorrhea reported to EudraVigilance after the administration of Comirnaty and Spikevax.

Overall, the PRAC considered that the available data does not support causal association and an update of the product information for either vaccine.

The committee will continue to carefully monitor this issue and has requested the marketing authorisation holders to include it in the next periodic safety update reports (PSURs) for Comirnaty and Spikevax.

New safety information for healthcare professionals

As part of its advice on safety-related aspects to other EMA committees, the PRAC discussed direct healthcare professional communications (DHPCs) containing important information for Neofordex and Xalkori.

Neofordex: change of tablet due to risk of possible stability issues and reduced efficacy

This DHPC informs healthcare professionals of the removal of the score-line on Neofordex (dexamethasone) tablets.

The marketing authorisation holder will produce new tablets without a score-line down the middle and with a 40 mg imprint on one side. By removing the score-line, and consequently the possibility to split the tablet into equal halves, it will only allow administration of 40 mg.

Neofordex is a medicine used together with cancer medicines to treat adults with multiple myeloma who have developed symptoms. Multiple myeloma is a cancer of a type of white

blood cell called plasma cells, which are part of the immune system.

Neofordex is available as 40 mg tablets and the usual dosage is 40 mg once a day. However, the dosage and how frequently a patient takes Neofordex vary depending on the medicines it is given with and the patient's condition.

For elderly and/or frail patients, or when the therapeutic protocol of associated treatment requires it, the daily dose may be reduced to 20 mg. In addition, at the end of dexamethasone treatment, the dose should be reduced gradually until a complete stop.

Stability issues, due to sensitivity to humidity, are a particular concern if tablets are being halved to adjust dosing. Patients could be exposed to a product of lesser quality and potential reduction in efficacy if the halved tablet is not adequately discarded.

When treating elderly and/or frail patients, or other patients for who the dose of dexamethasone needs to be reduced to 20 mg, and at the end of treatment, physicians are recommended to prescribe other products containing a lower dose of dexamethasone.

Patients should be informed and specifically advised not to cut tablets, and to store the tablets in the original blisters until they use them.

Xalkori: Vision disorders, including risk of severe visual loss, need for monitoring in paediatric patients

This DHPC informs healthcare professionals of the risk of ocular toxicity, severe visual loss and the need for monitoring in paediatric patients with Xalkori.

Xalkori (crizotinib) is a cancer medicine used to treat adults with a type of lung cancer called non-small cell lung cancer (NSCLC), when the disease is advanced. Xalkori has been studied in children from 6 to 18 years of age as a monotherapy for the treatment of relapsed or refractory systemic anaplastic large cell lymphoma (ALCL) that is ALK positive or patients with unresectable, recurrent, or refractory ALK positive inflammatory myofibroblastic tumour (IMT).

Vision disorders have been reported in 61% of paediatric patients treated with crizotinib in clinical trials for these indications.

Vision disorders and ocular toxicity are more challenging to detect in children. Young patients may not report or notice changes in vision without specific questioning of symptoms and examinations. Paediatric patients should be monitored for ocular toxicity, including the risk of severe vision loss. They should receive a baseline ophthalmologic examination prior to starting Xalkori with follow-up examinations. Healthcare professionals are advised to inform patients and caregivers of the symptoms and remind them to contact their doctor if any of these symptoms develop. Any visual symptoms should be referred to an eye specialist.

Healthcare professionals are also advised to consider a dose reduction of Xalkori for patients who develop Grade 2 ocular disorders. If Grade 3 and 4 ocular disorders occur, treatment with the medicine should be discontinued permanently, unless another cause is identified.

The product information and the educational material for patients and caregivers have been updated with instructions/recommendations in children about the risk of ocular toxicity, including severe vision loss.

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

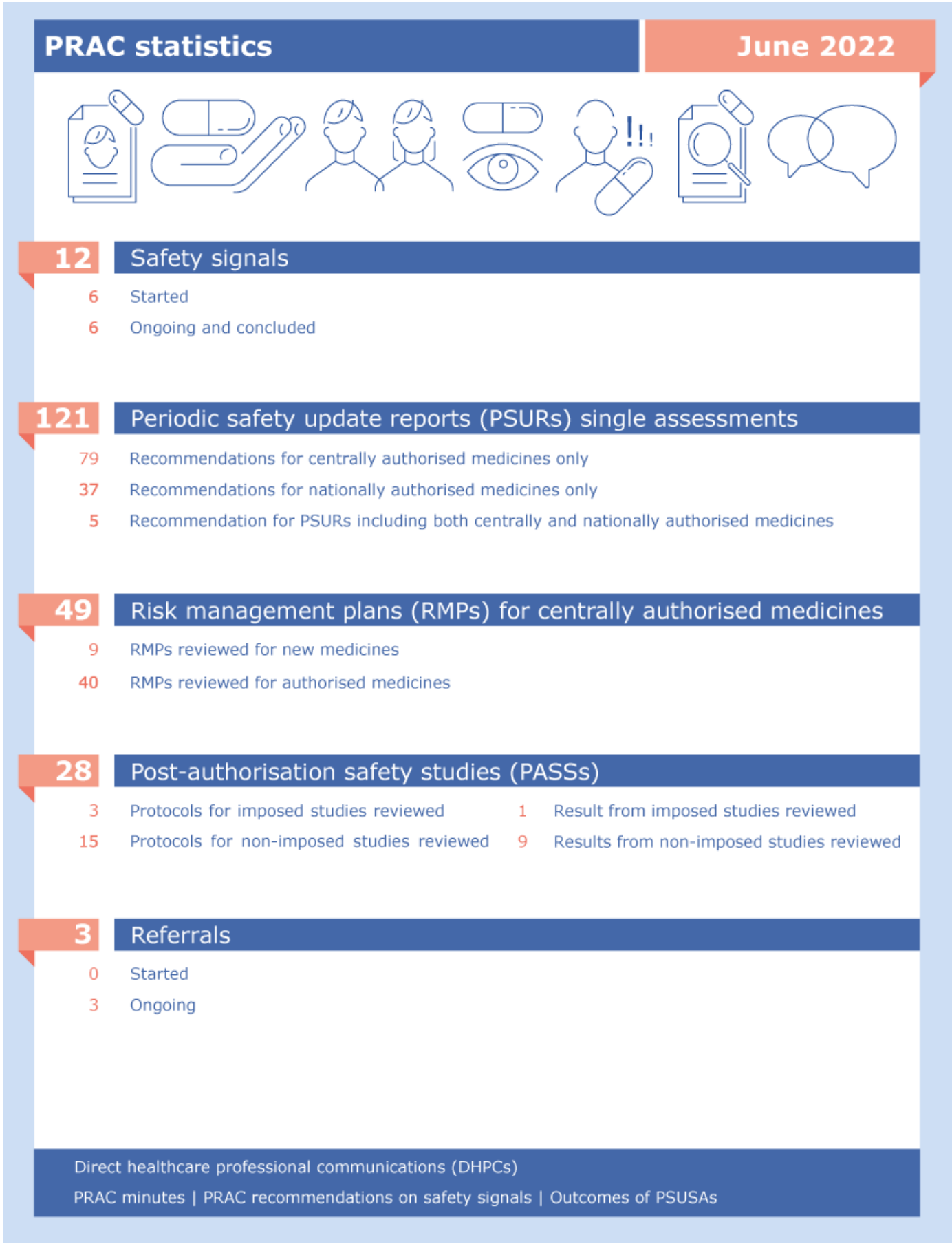
Agenda

Agenda - PRAC draft agenda of meeting 7-10 June 2022 (PDF/728.42 KB) (new)

Draft

First published: 07/06/2022
EMA/PRAC/246158/2022

PRAC statistics: June 2022



PRAC statistics: June 2022 (PDF/802.12 KB) (new)

First published: 10/06/2022

Glossary:

- **Safety signal assessments**. A safety signal is information which suggests a new potentially causal association, or a new aspect of a known association between a medicine and an adverse event that warrants further investigation. Safety signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. More information can be found under 'Signal management'.
- **Periodic safety update reports**, abbreviated as PSURs, are reports prepared by the marketing authorisation holder to describe the worldwide safety experience with a medicine in a defined period after its authorisation. PSURs for medicinal products that contain the same active substance or the same combination of active substances but have different marketing authorisations and are authorised in different EU Member States, are jointly assessed in a single assessment procedure. More information can be found under 'Periodic safety update reports: questions and answers'.
- **Risk management plans**, abbreviated as RMPs, are detailed descriptions of the activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicines. Companies are required to submit an RMP to EMA when applying for a marketing authorisation. RMPs are continually updated throughout the lifetime of the medicine as new information becomes available. More information is available under 'Risk-management plans'.
- **Post-authorisation safety studies**, abbreviated as PASSs, are studies carried out after a medicine has been authorised to obtain further information on its safety, or to measure the effectiveness of risk-management measures. The PRAC assesses the protocols (aspects related to the organisation of a study) and the results of PASSs. More information can be found under 'Post-authorisation safety studies'.
- **Referrals** are procedures used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral related to safety of medicines, the PRAC is requested by a Member State or the European Commission to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. More information can be found under referral procedures.
- **Summary safety reports** have been introduced as part of the enhanced safety monitoring of COVID-19 vaccines. Marketing authorisation holders are required to submit these reports to EMA, starting on a monthly basis. Their submission complements the submission of PSURs. For more information see EMA's pharmacovigilance plan for COVID-19 vaccines.

Ongoing referrals

Janus Kinase inhibitors (JAKi) – Article 20 Referral
Under evaluation
PRAC continued its assessment
Nomegestrol and chlormadinone - Article - 31 Referral

Under evaluation
PRAC continued its assessment
Terlipressin-containing medicinal products-Article 31 Referral
Under evaluation
PRAC continued its assessment

Related content

- Amfepramone-containing medicinal products: Article 31 referrals

Related content

- EMA recommends withdrawal of marketing authorisation for amfepramone medicines (10/06/2022)
- Safety of COVID-19 vaccines
- COVID-19 vaccines: authorised
- PRAC: Agendas, minutes and highlights
- Pharmacovigilance Risk Assessment Committee (PRAC): 7-10 June 2022

Related documents

Acronyms and abbreviations used in PRAC minutes (PDF/223.84 KB)

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