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) 7-10 March 2022

COVID-19 Vaccine Janssen: small vessel vasculitis added as a side effect

EMA's medicines safety committee (PRAC) has recommended that small vessel vasculitis with cutaneous manifestations (inflammation of blood vessels in the skin which may result in a rash, pointed or flat, red spots under the skin's surface and bruising) should be added to the product information of COVID-19 Vaccine Janssen as a possible side effect of unknown frequency.

Small vessel vasculitis can be caused by viral or bacterial infections as well as by medicines and vaccines. Generally, manifestations of the disease spontaneously resolve over time with appropriate supportive care.

PRAC has reviewed a total of 21 cases reported globally in the context of the latest summary safety report, including 10 cases consistent with the established definition of single organ cutaneous vasculitis (vasculitis affecting a single organ). For most of these 10 cases no other obvious explanation was identified; eight of these cases occurred soon after the administration of the vaccine.

As of 31 December 2021, approximately 42.5 million doses of the vaccine had been administered worldwide.

The PRAC will continue to monitor for cases of vasculitis and will communicate further if new information becomes available.

Spikevax: new warning for flare-ups of capillary leak syndrome

The PRAC has recommended that a warning for flare-ups of capillary leak syndrome (CLS) should be added to the product information for the COVID-19 vaccine Spikevax.

CLS is an extremely rare, serious condition that causes fluid leakage from small blood vessels (capillaries), resulting in rapid swelling of the arms and legs, sudden weight gain, feeling faint, thickening of the blood, low blood levels of albumin (an important blood protein) and low blood pressure. CLS is frequently related to viral infections, some blood cancers, inflammatory diseases and some treatments.

The PRAC assessed all the available data as well as all the cases of CLS reported in the Eudravigilance database after the administration of the mRNA vaccines Spikevax and Comirnaty.

The Committee concluded that there was insufficient evidence to establish a causal association between the two vaccines and the onset of new cases of CLS. However, the PRAC recommended the inclusion of a warning in the product information for Spikevax to raise awareness of the potential risk of flare-ups among healthcare professionals and patients. The Committee recommended this warning as some cases of flare-ups of CLS pointed towards an association with Spikevax, while the cases reported after vaccination with Comirnaty did not support such association.

Healthcare professionals should be aware of the signs and symptoms of CLS and of a possible risk of flare-ups in people with a history of CLS. Vaccinated individuals with a history of CLS should consult their treating physician when planning their vaccination.

In total 55 reported cases of CLS were reviewed, 11 with Spikevax and 44 with Comirnaty. Global exposure at the time of the assessment was estimated at approximately 559 million doses for Spikevax and 2 billion doses for Comirnaty.

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 safety information for dexmedetomidine.

Dexmedetomidine: Increased risk of mortality in intensive care unit patients aged 65 years and less

This DHPC aims to inform healthcare professionals of the increased risk of mortality when administering dexmedetomidine in intensive care unit (ICU) patients aged 65 years and less, compared with alternative sedatives.

Dexmedetomidine is a medicine authorised for light sedation (a state of calm or feeling sleepy) of adult patients in ICUs, allowing the patient to stay awake and respond to verbal stimulation for diagnostic or surgical procedures.

SPICE III study was a randomised clinical trial comparing the effect of sedation with dexmedetomidine on all-cause mortality (deaths from any cause) with the effect of usual standard of care in 3,904 critically ill adult ICU patients in need of mechanical ventilation. The study showed no difference in the overall 90-day mortality between dexmedetomidine and alternative sedatives (propofol, midazolam). However, dexmedetomidine was associated with an increased risk of mortality in patients aged 65 years and less, compared with alternative sedatives.

The product information for dexmedetomidine is being updated with a warning describing the evidence and risk factors. Healthcare professionals are being advised to weigh these findings against the expected clinical benefit of dexmedetomidine compared to alternative sedatives in this age group.

The DHPC for dexmedetomidine will be forwarded to EMA's human medicines committee, the 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.

PRAC statistics: March 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

Procedure	Status	Update
Amfepramone-containing medicinal products – Article - 31 Referral	Under evaluation	PRAC continued its assessment.
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.