



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) 5-8 February 2024

Paxlovid: reminder of serious adverse reactions when taken together with certain immunosuppressants

EMA's safety committee (PRAC) is reminding healthcare professionals of the risk of serious and potentially fatal adverse reactions with Paxlovid (nirmatrelvir, ritonavir) when used in combination with certain immunosuppressants that have a narrow safe dosage range (where small changes in the dose can lead to serious adverse reactions), due to drug-drug interactions reducing the body's ability to eliminate these medicines.

Paxlovid is a medicine used for treating COVID-19 in adults who do not require supplemental oxygen and who are at increased risk of the disease becoming severe. The immunosuppressants concerned are called calcineurin inhibitors (tacrolimus, ciclosporin) and mTOR inhibitors (everolimus, sirolimus), which reduce the activity of the immune system. They are used for treating certain autoimmune disorders or for preventing the body from rejecting transplanted organs.

Paxlovid should only be given with tacrolimus, ciclosporin, everolimus or sirolimus if close and regular monitoring of their blood levels is possible, to reduce the risk of drug-drug interactions causing serious reactions. Healthcare professionals need to consult with a multidisciplinary group of specialists to manage the complexity of taking these medicines together.

Paxlovid must not be given in combination with medicines for which elimination from the body is highly reliant on a set of liver enzymes (proteins), known as CYP3A, and that also have a narrow safe dosage range. This includes the immunosuppressant called voclosporin. Before starting the treatment with Paxlovid, healthcare professionals should carefully weigh the potential benefits of Paxlovid treatment against the risks of serious adverse reactions in case of administration together with immunosuppressants.

The PRAC reviewed all available evidence, including reports of serious adverse reactions, some of which were fatal, resulting from drug-drug interactions between Paxlovid and these immunosuppressants. In several cases, blood levels of these immunosuppressants increased rapidly to toxic levels resulting in life-threatening conditions. Therefore, the PRAC agreed on a direct healthcare professional communication (DHPC) to remind healthcare professionals of the risk of these interactions, which is known and already described in the product information for this medicine.



The DHPC for Paxlovid will be forwarded to EMA's human medicines committee (CHMP). When adopted, 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: February 2024

[infographic]

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
Hydroxyprogesterone-containing medicinal products – Article-31 referral	Under evaluation	PRAC continued its assessment.

Notes

1. This press release, together with all related documents, is available on the Agency's website at: www.ema.europa.eu
2. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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