3 April 2024
EMA/535476/2023

EMA confirms measures to minimise the risk of serious side effects with medicines containing pseudoephedrine

On 25 January 2024, EMA's human medicines committee (CHMP) endorsed the measures recommended by the Pharmacovigilance Risk Assessment Committee (PRAC) to minimise the risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) for medicines containing pseudoephedrine.

PRES and RCVS are rare conditions that can involve reduced blood supply to the brain, potentially causing serious, life-threatening complications. With prompt diagnosis and treatment, symptoms of PRES and RCVS usually resolve.

CHMP confirmed that medicines containing pseudoephedrine are not to be used in patients with high blood pressure that is severe or uncontrolled (not being treated or resistant to treatment) or in patients with severe acute (sudden) or chronic (long-term) kidney disease or failure.

In addition, healthcare professionals should advise patients to stop using these medicines immediately and seek treatment if they develop symptoms of PRES or RCVS, such as severe headache with a sudden onset, feeling sick, vomiting, confusion, seizures and visual disturbances.

The recommendations follow a review of all available evidence, including post-marketing safety data, which concluded that pseudoephedrine is associated with risks of PRES and RCVS. During the review, PRAC sought advice from an expert group of general practitioners, otorhinolaryngologists (specialists in diseases of the ear, nose, throat, head and neck), allergologists (specialists in the treatment of allergies) and a patient representative. PRAC also considered information submitted by a third party representing healthcare professionals.

The product information for all pseudoephedrine-containing medicines will be updated to include the risks concerning PRES and RCVS and the new measures to be taken. Restrictions and warnings are already included in the product information of these medicines to reduce cardiovascular and cerebrovascular ischaemic (involving reduced blood supply to the heart and brain) risks.

The CHMP opinion was sent to the European Commission, which issued legally binding decisions across the EU on 25 and 27 March 2024.

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Information for patients

- An EU-wide review has found that pseudoephedrine-containing medicines can cause posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS), rare conditions that can involve reduced blood supply to the brain. This follows an evaluation of all available data including few reported cases of these conditions.
- Do not take pseudoephedrine-containing medicines if you have high blood pressure that is severe or uncontrolled (not being treated or resistant to treatment) or if you have severe acute (sudden) or chronic (long-term) kidney disease or failure, as these are risk factors for developing PRES or RCVS.
- Stop using pseudoephedrine-containing medicines immediately and seek urgent medical assistance if you develop symptoms of PRES or RCVS such as a severe headache with a sudden onset, feeling sick, vomiting, confusion, seizures and changes in vision.
- If you have any questions or concerns about your medicines, speak to your doctor or pharmacist.

Information for healthcare professionals

- An EMA review has found that pseudoephedrine-containing medicines are associated with risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS), serious conditions affecting the cerebral blood vessels. This follows an evaluation of all available data including few reported cases of these conditions.
- There were no fatal cases of PRES or RCVS reported, and most of the cases resolved following discontinuation of the medicine and appropriate treatment.
- Pseudoephedrine-containing medicines must not be used in patients with severe or uncontrolled hypertension or severe acute or chronic kidney disease or renal failure, as these are risk factors for developing PRES or RCVS.
- Patients should be advised to discontinue treatment and seek immediate medical assistance if they develop symptoms of PRES or RCVS such as sudden, severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances.
- The risks of PRES and RCVS should be considered alongside other risks associated with pseudoephedrine-containing medicines, including cardiovascular or ischaemic events.

A direct healthcare professional communication (DHPC) has been sent to relevant healthcare professionals. The DHPC is also published on EMA's website.

More about the medicine

Pseudoephedrine works by stimulating nerve endings to release the chemical noradrenaline, which causes the blood vessels to constrict (narrow). This reduces the amount of fluid released from the vessels, resulting in less swelling and less mucus production in the nose.

Pseudoephedrine-containing medicines are authorised in various EU Member States and are used alone or in combination with other medicines to treat symptoms of cold and flu, such as headache, fever and pain, allergic rhinitis (inflammation of the nasal passages from allergies) or vasomotor rhinitis (inflammation of the nasal passages from non-allergic or non-infectious causes), in people with nasal congestion. Pseudoephedrine is also authorised in some EU Member States to treat aerotitis

(inflammation of the middle ear due to sudden changes in air pressure) in a fixed-dose combination with triprolidine.

Within the EU, pseudoephedrine-containing medicines are available under various trade names including Actifed, Aerinaze, Aspirin Complex, Clarinase, Humex rhume, and Nurofen Cold and Flu.

More about the procedure

The review of pseudoephedrine-containing medicines was initiated at the request of the French medicine agency, under Article 31 of Directive 2001/83/EC.

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC recommendations were sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion.

The CHMP opinion was forwarded to the European Commission, which issued final legally binding decisions applicable in all EU Member States on 25 and 27 March 2024.