SAFETY ALERT

DRAP SAFTEY ALERT NO. 49

Safety Alert of Risk of Posterior Reversible Encephalopathy Syndrome (PRES) and Reversible Cerebral Vasoconstriction Syndrome (RCVS) with Pseudoephedrine-Containing Medicines.

Date: 27th of April, 2024.

Target Audience.

- Manufacturers and importers of pseudoephedrine-containing medicines;
- Healthcare Professionals; and
- Patients, Consumers or Caregivers.

Background.

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicine Agency (EMA) in its meeting held on 27-30th November 2023 recommended new measures for medicines containing pseudoephedrine to minimize the risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) and informed that product information for all pseudoephedrine-containing medicines will be updated to include the risks. 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. It was recommended 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 with severe acute (sudden) or chronic (long-term) kidney disease or failure. In addition, as part of its advice on safety-related aspects to other EMA committees, the PRAC discussed a direct healthcare professional communication (DHPC) with important information on pseudoephedrine-containing products which was also forwarded to EMA's human medicines committee (CHMP).

RES 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. 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.

NPC, DRAP, PM Health Complex, Chak Shahzad Islamabad +92 51 9255981 npc@dra.gov.pk

On 25 January 2024, EMA's Committee for Medicinal Products for Human Use (CHMP) endorsed the measures recommended by the PRAC to minimise the risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) for medicines containing pseudoephedrine. 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. The CHMP opinion has been sent to the European Commission, which will issue a legally binding decision across the EU.

Action in Pakistan.

The case was discussed in the 4th meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the DRAP held on 26th of February, 2024 which decided the case as per Rule 10 (1) (h) (iv) of the Pharmacovigilance Rules, 2022 that registration holders should update the warning and precaution section of the prescribing information/label of pseudoephedrine-containing medicines by including information about the risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) along with advise 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 with severe acute (sudden) or chronic (long-term) kidney disease or failure. Similarly, as per Rules 10 (1) (h) (vi) registration holders were advised to issue direct healthcare professionals communication by highlighting the risk.

Therapeutic Goods.

Name: Pseudoephedrine is a stimulant that is often used as a decongestant in people who have a cold or allergies.

Advice for Healthcare Professionals.

Healthcare professionals are informed that a review has found that pseudoephedrine-containing medicines are associated with risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS), a serious condition affecting the cerebral blood vessels. This follows an evaluation of all available data including a few reported cases of these conditions. There were no fatal cases of PRES or RCVS reported internationally, and most of the cases were resolved following discontinuation of the medicine and appropriate treatment. Healthcare professionals are advised that 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.

Advice for Patients.

Patients are advised not to take pseudoephedrine-containing medicines if they have high blood pressure that is severe or uncontrolled (not being treated or resistant to treatment) or if they have severe acute (sudden) or chronic (long-term) kidney disease or failure, as these are risk factors for developing PRES or RCVS. Patients are also advised to stop using pseudoephedrine-containing medicines immediately and seek urgent medical assistance if they develop symptoms of PRES or RCVS such as a severe headache with a sudden onset, feeling sick, vomiting, confusion, seizures and changes in vision.

Guidelines for reporting Adverse Drug Reactions (ADRs).

Both healthcare professionals and patients are requested to report any suspected adverse drug reaction (ADRs) with pseudoephedrine-containing medicines to the National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan (DRAP) through the Med Vigilance E-Reporting System available on the DRAP website. Similarly, ADRs can also be reported through Med Safety App which is available for download from the App Store (for iOS devices) and Google Play (for Android devices).

References.

- Minutes of the 4th meeting of the Pharmacovigilance Risk Assessment Expert Committee.
- Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 27-30 November 2023.
- Pseudoephedrine-containing medicinal products - referral, EMA.