Direct Healthcare Professional Communication

Pseudoephedrine – Risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)

Dear Healthcare professional,

<Name of marketing authorisation holder> in agreement with <the European Medicines Agency> and the <National competent authority> would like to inform you of the following:

Summary

- **Few cases of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) have been reported with the use of pseudoephedrine-containing medicines.**

- **Pseudoephedrine-containing medicines are contraindicated in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease or renal failure, as these conditions increase the risks of PRES or RCVS.**

- **Symptoms of PRES and RCVS include sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances.**

- **Patients should be advised to immediately stop using these medicines and seek medical assistance if signs or symptoms of PRES or RCVS develop.**

Background on the safety concern

Pseudoephedrine is authorised, alone or in combination with other substances, for short-term symptomatic relief of nasal or sinus congestion caused by the common cold or allergic rhinitis <or vasomotor rhinitis><or aerotitis>.

Cases of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS), which are serious conditions affecting the cerebral blood vessels, have been reported in patients taking pseudoephedrine-containing medicines. Most reported cases resolved following discontinuation and appropriate treatment. No fatal cases of PRES or RCVS have been reported.

Following an EU-wide review of reported cases and other available data to evaluate the risks of PRES and RCVS with pseudoephedrine-containing medicines, it has been concluded that pseudoephedrine is associated with risks of PRES and RCVS and that the product information should be updated to include information on these adverse reactions and measures to reduce the risks.

The newly identified risks of PRES or RCVS should be considered in the context of the overall safety profile of pseudoephedrine, which also includes other cardiovascular and cerebrovascular ischaemic events.

Overview of PRES and RCVS

PRES can manifest with a wide variety of acute or subacute neurological symptoms, including headache, mental status alteration, seizures, visual disturbances and/or focal neurologic deficits. An acute or sub-acute onset of the symptoms (hours to days) is typical. PRES is usually reversible; symptoms cease within several days or weeks with the reduction of blood pressure and withdrawal of causative drugs.

RCVS usually manifests with thunderclap headache (severe pain peaking in seconds), typically bilateral, with posterior onset followed by diffuse pain frequently accompanied by nausea, vomiting, photophobia and phonophobia. Transient focal deficits can be present in some patients. Ischaemic and haemorrhagic stroke are the major complications of the syndrome.

Call for reporting

Please report any suspected adverse reactions associated with the use of pseudoephedrine in accordance with the national requirements via the national spontaneous reporting system, to:

<Details (e.g., name, postal address, fax number, website address) on how to access the national spontaneous reporting system>

Company contact point

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>

Communication plan for Direct Healthcare professional communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Pseudoephedrine-containing medicinal products
Marketing authorisation holder(s)	All concerned marketing authorisation holders of pseudoephedrine-containing medicinal products. All concerned marketing authorisation holders in each Member State are strongly encouraged to collaborate, so that a single DHPC is prepared and circulated in each Member State. The letter circulated in each Member State should cover all active substance-containing products authorised in that Member State. It is encouraged that the originator marketing authorisation holder (where available) in each Member State acts as the contact point for the national competent authority, on behalf of the other concerned marketing authorisation holders in the same Member State. If no originator product is marketed in the Member State, it is encouraged that one of the concerned generic companies acts as contact point for the competent authority.
Safety concern and purpose of the communication	Risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) and measures to minimise these risks.
DHPC recipients	General practitioners, allergologists, otorhinolaryngologists, pharmacists, neurologists, emergency physicians, pneumologists. The list of recipients should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU member states where pseudoephedrine-containing medicinal products are authorised and marketed.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	30 Nov 2023
DHPC and communication plan (in English) agreed by CHMP	25 Jan 2024
Submission of translated DHPCs to the national competent authorities for review	CHMP opinion + 5 calendar days
Agreement of translations by national competent authorities	CHMP opinion + 10 calendar days
Dissemination of DHPC	CHMP opinion + 15 calendar days