

## **IMPORTANT MEDICINE SAFETY INFORMATION**

30 May 2024

### **PSEUDOEPHEDRINE-CONTAINING MEDICINES– RISK OF POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) AND REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME (RCVS)**

**Dear Healthcare Professional,**

Acino Pharma (Pty) Ltd, Adcock Ingram Limited, Aspen Pharmacare, Cipla Medpro, Ranbaxy Pharmaceuticals (Pty) Ltd and Pharmaceutical Contractors (Pty) Ltd, in collaboration with the South African Health Products Regulatory Authority (SAHPRA), would like to draw your attention to the risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) associated with the use of pseudoephedrine-containing medicines.

#### **Summary**

- A 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 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.
- 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 medicines.
- RCVS usually manifests with a 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.

- 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.
- The Professional Information (PI) and Patient Information Leaflets (PILs) for pseudoephedrine-containing medicines listed below will be updated to appropriately reflect the above safety information.

#### **Advice for healthcare professionals to provide to patients:**

- Healthcare professionals should inform patients that pseudoephedrine-containing medicines are for short-term use only and should not be used for prolonged or extended use. Patients should be encouraged to follow the instructions for use in the PIL.
- Patients should be alerted about the risks, signs and symptoms of PRES and RCVS associated with the use of pseudoephedrine-containing medicines.
- Healthcare professionals should advise patients to immediately stop taking pseudoephedrine-containing medicines and seek urgent medical assistance if they experience severe headache that develops very quickly or suddenly feeling sick or are vomiting, confused or experiencing seizures or changes in vision.
- Patients should be advised not to take pseudoephedrine-containing medicines if they have very high blood pressure (hypertension) or uncontrolled hypertension, severe acute (sudden) or chronic (long-term) kidney disease or kidney failure. Patients should seek guidance from their doctor or pharmacist if they are unsure about the symptoms experienced after taking these medicines.
- Patients should be made aware that non-serious side effects, which are typically mild, may be experienced, while using any medicine. Healthcare professionals should emphasise to patients, the importance of using the PIL for guidance and seeking advice from a doctor or pharmacist if they are experiencing side effects associated with the use of pseudoephedrine-containing medicines.

#### **Advice to Healthcare professionals:**

- Healthcare professionals are reminded that medicines containing pseudoephedrine are for short term use only and should not be used for prolonged or extended use.
- PRES and RCVS are recognised very rare side effects with pseudoephedrine-containing medicines. These risks present with the following symptoms: sudden severe headache or thunderclap headache, sudden onset of nausea and vomiting, confusion, seizures and/or visual disturbances.
- 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.
- If signs and symptoms suggestive of PRES and RCVS, pseudoephedrine-containing medicines should be withdrawn immediately, and an alternative treatment considered (as appropriate).
- If a patient has developed PRES and RCVS with the use of pseudoephedrine-containing medicines, treatment with these medicines must not be restarted at any time.

- Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality problems associated with the use of pseudoephedrine-containing products listed below to SAHPRA by completing an ADR reporting form accessible via this link <https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/> and email it to [adr@sahpra.org.za](mailto:adr@sahpra.org.za).
- Alternatively, healthcare professionals may use the following eReporting link <https://primaryreporting.who-umc.org/ZA> available on the SAHPRA website ([www.sahpra.org.za](http://www.sahpra.org.za)).
- Additionally, reporting can be done via the Med Safety App. The App can be downloaded into a smart mobile phone through Google Play or App Store. For more information on Med Safety App, please use the following link: <https://medsafety.sahpra.org.za/>.
- For more information on ADR reporting of the products listed below, please contact the SAHPRA Pharmacovigilance unit at [pvqueries@sahpra.org.za](mailto:pvqueries@sahpra.org.za) or use company contact details indicated below:

Table 1: Company pseudoephedrine-containing products and contact details:

Company	Product name	Registration Number	Contact details
Acino Pharma (Pty) Ltd	Decofed Syrup Decofed Tablets	Y/5.8/137 Y/5.8/136	Tel:+27 516 1700 Drug Safety number:+27 60 998 7896 <a href="mailto:Drugsafety_ZA@acino.swiss">Drugsafety_ZA@acino.swiss</a>
Adcock Ingram Limited	Adco-Tussend Syrup Adco-Flupain Syrup Colcaps Children Syrup Corenza Cold and Flu Syrup	27/10.1/0256 27/5.8/0260 D/5.8/0054 37/5.8/0552	Tel:+27 11 635 0134 Safety number:+27 73 540 7052 <a href="mailto:Adcock.Aereports@adcock.com">Adcock.Aereports@adcock.com</a>
Cipla Medpro	Coryx Paediatric Syrup Coryx Tablets Coryx Cough and Cold Solution	31/5.8/0056 27/5.8/0435 27/10.1/0490	Praba Thandrind <a href="mailto:Praba.Thandrind@Cipla.com">Praba.Thandrind@Cipla.com</a> <a href="mailto:drugsafetysa@cipla.com">drugsafetysa@cipla.com</a> Tel: 021 943 4200
Ranbaxy Pharmaceuticals (Pty) Ltd	Trifen Expect Paediatric solution Betafed Syrup	27/10.1/0536 31/5.8/0249	<a href="mailto:Geeta.Ghela@sunpharma.com">Geeta.Ghela@sunpharma.com</a>
Aspen Pharmacare	Sinuclear Paediatric Syrup/Stroop Flusin-C Syrup Sinugesic Tablets Flusin S Effervescent Tablets Acuflu P Syrup	30/5.8/0053 27/5.8/0523 34/5.8/0196 30/5.8/0001 X/5.8/9	<a href="mailto:Drugsafety@aspenpharma.com">Drugsafety@aspenpharma.com</a>
Pharmaceutical Contractors (Pty) Ltd	Ibumax Cold and Flu tablets	A40/5.8/0218	<a href="mailto:claudem@pharmacon.co.za">claudem@pharmacon.co.za</a>

Yours faithfully,

Shaistha Sing Responsible Pharmacist Acino Pharma (Pty) Ltd  Signature	Nikola Whelan Responsible Pharmacist Aspen Pharmacare  Signature
Tammy Gopal Responsible Pharmacist Adcock Ingram Limited  Signature	Praba Thandrind Responsible Pharmacist Cipla Medpro  Signature
Geeta Ghela Responsible Pharmacist/QA Head Ranbaxy Pharmaceuticals (Pty) Ltd <a href="mailto:Geeta.Ghela@sunpharma.com">Geeta.Ghela@sunpharma.com</a>  Signature  Pitchai Pandikumar Pharmacovigilance Manger <a href="mailto:Pitchai.pandikumar@sunpharma.com">Pitchai.pandikumar@sunpharma.com</a>  Signature	Claude Martins Responsible Pharmacist Pharmaceutical Contractors (Pty) Ltd  Signature

#### References

1. SAHPRA Letter dated 05 March 2024 Re: Pseudoephedrine – risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (PCVS)
2. [Pseudoephedrine: very rare risk of posterior reversible encephalopathy syndrome \(PRES\) and reversible cerebral vasoconstriction syndrome \(RCVS\) - GOV.UK \(www.gov.uk\)](#)
3. [Pseudoephedrine-containing medicinal products - referral | European Medicines Agency \(europa.eu\)](#)