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# IMPORTANT MEDICINE SAFETY INFORMATION

21 May 2024

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

## Dear Healthcare professional,

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), Johnson and Johnson (Pty) Ltd would like to inform you about the risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) associated with the use of pseudoephedrine-containing medicines.

**Summary**

- 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, allergic rhinitis, 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

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causative medicines.

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.

Cases of PRES and 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.

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

- Healthcare professionals should inform patients that pseudoephedrine-containing medicines are for short-term use only, used to relieve symptoms of nasal and sinus congestion with colds, flu and allergies. Patients should be reminded to follow the instructions for use in the Patient Information Leaflet (PIL).
- Patients should be alerted about the risks of PRES and RCVS associated with the use of pseudoephedrine-containing medicines. Healthcare professionals should notify patients about PRES and RCVS cases reported with the use of these medicines, and also that, PRES and RCVS are rare conditions that can involve inflammation and/or reduced blood supply to the brain.
- Healthcare professionals should advise patients to stop taking pseudoephedrine-containing medicines and seek urgent medical attention if they experience severe headache that develops very quickly or suddenly feel sick or are vomiting, confused or experiencing seizures or changes in vision.
- Patients should be warned not to take pseudoephedrine-containing medicines if they have very high blood pressure (hypertension) or uncontrolled hypertension.
- Furthermore, patients are to be advised not take pseudoephedrine-containing medicines if they have severe acute (sudden) or chronic (long-term) kidney disease or kidney failure. Patients should be encouraged to seek advice from their doctor or pharmacist if they are unsure about the symptoms experienced after taking these medicines.
- Patients should be enlightened that they may experience non-serious side effects, which are typically mild, while using any medicine. Healthcare professionals should emphasise the importance of using the Patient Information Leaflet 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 pseudoephedrine-containing medicines are for short

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term use only and should not be used for prolonged or extended use.

- 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 the products listed below to Johnson and Johnson, or to SAHPRA via the following eReporting link https://primaryreporting.who-umc.org/ZA available on the SAHPRA website (www.sahpra.org.za).

- Alternatively, healthcare professionals may complete 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.

- 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 products listed below, please contact the SAHPRA Pharmacovigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details indicated below:

**Company contact points.**

| | |
|---|---|
| Responsible Pharmacist: Sello Malete<br>Email: SMalet01@kenvue.com<br>Tel: 021 490 0484 | Pharmacovigilance: Bonita Petersen<br>Email: pharmacovigssa@kenvue.com<br>Tel: 021 490 0440 |

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Company products

| Product | Active ingredients | Registration Number |
|---|---|---|
| Benylin Daytime Flu Tablets | Ibuprofen; Pseudoephedrine hydrochloride | 36/5.8/0206 |
| Benylin Four Flu Liquid | Diphenhydramine hydrochloride; Paracetamol; Pseudoephedrine hydrochloride | 33/5.8/0345 |
| Benylin Four Flu Tablets | Diphenhydramine hydrochloride; Paracetamol; Pseudoephedrine hydrochloride | 33/5.8/0509 |
| Sinumax Allergy Sinus Caplets | Chlorphenamine maleate; Paracetamol; Pseudoephedrine hydrochloride | 31/5.8/0555 |
| Sinutab 3-Way | Ibuprofen; Pseudoephedrine hydrochloride | 36/5.8/0207 |
| Sinutab Sinus Allergy Congestion & Pain | Chlorphenamine maleate; Paracetamol; Pseudoephedrine hydrochloride | 37/5.8/0260 |
| Sinutab Sinus Pain Extra Strength | Chlorphenamine maleate; Codeine phosphate; Paracetamol; Pseudoephedrine hydrochloride | 37/5.8/0139 |
| Sinutab Sinus Pain Non-Drowsy | Paracetamol; Pseudoephedrine hydrochloride | 37/5.8/0138 |
| Sudafed Sinus Pain | Paracetamol; Pseudoephedrine hydrochloride | T/5.8/196 |
| Sinumax Tablets | Paracetamol; Pseudoephedrine hydrochloride | U/5.8/88 |

Yours Faithfully

**Signature:** Sello Malete

*Electronically signed by: Sello Malete*
*Reason: I am approving this document*
*Date: May 22, 2024 10:57 GMT+2*

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Sello Malete
Responsible Pharmacist

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