IMPORTANT MEDICINE SAFETY INFORMATION

Dear Healthcare Professional,

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

In collaboration with the South African Health Products Authority (SAHPRA), Bayer (Pty) Ltd would like to inform to 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

- Few cases of PRES and 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 the relief of nasal and ocular symptoms of upper respiratory mucosal congestion, as in allergic and vasomotor rhinitis.

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.

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;

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symptoms cease within several days or weeks with the reduction of blood pressure and withdrawal of 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.

The Professional Information (PI) and Patient Information Leaflets (PILs) for Bayer's pseudoephedrine-containing product, Clarityne Plus Repetabs®, will be updated to include PRES and RCVS as a warning and side effects.

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 of these medicines.

- Patients should be warned about the risks and symptoms of PRES and RCVS associated 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.

- Healthcare professionals should advise patients to immediately stop taking pseudoephedrine-containing medicines and seek urgent medical assistance if they experience symptoms mentioned above.

- Patients should be urged 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 these products.

- 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 as very rare side effects of pseudoephedrine-containing medicines. These products 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.

    - Alternatively, healthcare professionals may use the following eReporting link https://primaryreporting.who-umc.org/ZA available on the SAHPRA website (www.sahpra.org.za). Adverse reactions may aslo be reported through Bayer's eReporting portal, SafeTrack: https://www.safetrack-public.bayer.com

    - 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 or Bayer at pv.sewa@bayer.com.

Yours faithfully,
Bayer (Pty) Ltd

Eric Chauke
Responsible Pharmacist