NOVARTIS | Reimagining Medicine

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IMPORTANT MEDICINE SAFETY INFORMATION

TEGRETOL S® 100 MG/5 ML CARBAMAZEPINE SUSPENSION
UPDATE TO THE POSOLOGY AND METHOD OF ADMINISTRATION

03 September 2024

Dear Healthcare Provider / Professional.

Novartis South Africa (Pty) Ltd., the holder of the certificate of registration for Tegretol S® (carbamazepine) suspension, in agreement with the South African Health Products Regulatory Authority (SAHPRA), wishes to inform you about the following:

- Change in the maximum daily dose for Tegretol S® (carbamazepine) oral suspension due to the potential risks associated with ethylene glycol, which is a by-product of sorbitol (an excipient used in the product).

Summary

- Ethylene glycol (EG) has a permitted daily exposure (PDE) of 6.2 mg/day for adults as per the International Council on Harmonization (ICH) of Technical Requirements..
- Novartis conducted a portfolio review including Tegretol S® (carbamazepine) oral suspension to evaluate its products for excipients containing ethylene glycol (EG) do not exceed the defined PDE. It was observed that for Tegretol S® (carbamazepine) oral suspension, there is possibility of exceeding defined PDE when taken above 1200 mg/day in adult patients because of the quantity of sorbitol in the formulation. Sorbitol is one of the major potential sources of ethylene glycol (EG) because of its quantity in the formulation of Tegretol S® oral suspension.
- Novartis has implemented stricter limits for sorbitol which are lower than pharmacopeia limits in order to restrict ethylene glycol (EG) level. and hereby ensure that there is no risk of any batch potentially exceeding the ICH PDE during manufacturing.

- Additionally, to limit patient exposure to ethylene glycol (EG), Novartis proposes to limit the use of Tegretol® S oral suspension up to 1 200 mg/day as per the established clinical guidelines.
- There is no change proposed on the posology for Tegretol® tablets (immediate release and modified release) because they do not contain the sorbitol as an excipient.
- Currently, there are supply restrictions for sorbitol solution with the revised stricter limits. This might lead to potential shortage situations.

Tegretol S® 100 mg/5 ml (carbamazepine)

- Tegretol S® (carbamazepine) oral suspension is an antiepileptic medicine indicated for the treatment of epilepsy with motor and psychic manifestations:
  a) psychomotor or temporal-lobe epilepsy
  b) generalized tonic-clonic seizure
  c) mixed forms of seizures
  d) complex or simple partial seizures (with or without loss of consciousness) with or without secondary generalization.

  Also indicated for acute mania and maintenance treatment of bipolar affective disorders to prevent or attenuate recurrence, idiopathic trigeminal neuralgia, idiopathic glossopharyngeal neuralgia.
- The suspension is suitable for paediatric and adult patients who have difficulty in swallowing tablets or need initial careful adjustment of the dosage.
- Doses up to 1 600 mg/day for (carbamazepine) are recommended only in rare instances.

Sorbitol and ethylene glycol (EG)

- Sorbitol is a sugar alcohol used frequently in the food, pharmaceutical and beverage industry, due to its low sweetness and high solubility. It is an excipient used in Tegretol S® oral suspension as moistening agent.

Novartis confirms that the posology for formulations other than Tegretol S® oral suspension, remains unchanged. Patients can continue to receive doses of Tegretol® tablets up to 1 600 mg/day. The professional information (PI) and patient information leaflet (PIL) for Tegretol S® oral suspension will be/is updated to reflect a change in the maximum daily dose of Tegretol S® oral suspension alone to 1 200 mg/day.

Advice for healthcare professionals to provide to patients:

- Patients should be made aware about this safety information and counselled about possible options, such as switching Tegretol S® oral suspension to alternative treatment options, for continuation of treatment.

- If a switch in products is considered as an appropriate option, patients should be counselled to contact their physician immediately if they experience loss of seizure control and/or adverse effects after switching.

- Patients should be advised to make a habit of submitting prescriptions to the pharmacy seven days before they are due. This will enable the pharmacist to source other supplies if they are out of stock.

- Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality problems associated with the use of Tegretol S® oral suspension to SAHPRA via the following eReporting link https://primaryreporting.who-umc.org/ZA available on the SAHPRA website (www.sahpra.org.za).

- Furthermore, healthcare professionals may complete the ADR reporting form accessible on SAHPRA website 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.

- Reporting can also be done via the Med Safety App. The App can be downloaded into a smart phone through Google Play or App Store. For more information on the Med Safety App, please use the following link: https://medsafety.sahpra.org.za/.

- Alternatively, ADRs associated with Tegretol S® oral suspension can be reported to Novartis on the following email: patientsafety.sacg@novartis.com or via the website.

- Healthcare professionals may also contact Novartis on +27 860 929 929 for any questions about the information contained in this letter or the safe and effective use of Tegretol S® oral suspension.

Sincerely,

Sequeira Dylan

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