If undelivered please return to Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta

Ref: 07/2025/PLD
7th December 2025

Carbamazepine (Tegretol 100 mg/5ml Oral Suspension); restriction of use in neonates as concentration of the excipient, propylene glycol, exceeds recommended threshold

Dear Healthcare Professional,

Novartis Ireland Ltd. in agreement with Malta Medicines Authority would like to inform you of the following:

Summary

- Tegretol (carbamazepine) 100 mg/5ml Oral Suspension (OS) **should not be used in** neonates below 4 weeks of age (or 44 weeks post-menstrual age for pre-term babies).
- This is because of the amount of propylene glycol in the product, which may lead to serious adverse reactions such as metabolic acidosis, renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.
- The only exception is if no other treatment option is available and the expected benefit outweighs the risks. In such case, medical monitoring, including measurements of osmolar and/or anion gap, is recommended.
- If other carbamazepine oral suspensions without propylene glycol are available, they are not affected by this restriction of use.

Background on the safety concern

Tegretol (carbamazepine) 100 mg/5ml OS is indicated for the treatment of various conditions including epilepsy (generalised tonic-clonic and partial seizure types).

The concentration of propylene glycol, an excipient used in this formulation, is 25 mg/1 mL, which exceeds the recommended threshold for neonates of 1 mg/kg/day[1].
In neonates, doses of propylene glycol ≥1 mg/kg/day accumulate in the body due to immaturity of metabolic and renal clearance pathways of propylene glycol. This may lead to serious adverse reactions such as metabolic acidosis, renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

Therefore, Tegretol 100 mg/5ml Oral Suspension should not be used in neonates below 4 weeks of age for term babies (or 44 weeks post-menstrual age for pre-term babies). The only exception is if no other

[1] Questions and answers on propylene glycol used as an excipient in medicinal products for human use (EMA/CHMP/704195/2013)

treatment option is available and the expected benefit outweighs the risks, also considering the risks associated with the excipients.

Medical monitoring, including measurements of osmolar and/or anion gap, is recommended in neonates below 4 weeks of age who are receiving treatment with Tegretol 100 mg/ 5 ml Oral Suspension. Co-administration with other medicinal products containing propylene glycol or with any substrate of alcohol dehydrogenase such as ethanol increases the risk of propylene glycol accumulation and toxicity. The ethylene and diethylene glycol present in the product is also substrates of alcohol dehydrogenase.

The product information is being updated to reflect this limitation of use in neonates and to inform about the risk posed by the excipient content of the product.

For children above 4 weeks of age (or 44 weeks post menstrual age for preterm babies), there are no changes to the label recommendations. This update only affects Tegretol 100 mg/5ml Oral Suspension; no other Tegretol formulations or carbamazepine-containing products are impacted.

Call for reporting

Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Malta Medicines Authority ADR reporting form available online at http://medicinesauthority.gov.mt/adrportal and sent to Pharmacovigilance Section at Post-Licensing Directorate, Malta Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN or sent by email to: postlicensing.medicinesauthority@gov.mt

Healthcare Professionals may also report any adverse events associated with the use of Tegretol Oral Suspension (OS) to Novartis Pharma Services Inc., Representative Office, Malta, by phone on +356 21222872, online on www.novartis.com/report or by e-mail at drug_safety.malta@novartis.com

Company contact point

Company	Product Name	Email	Phone
Novartis Pharma Services Inc., Representative Office, Malta	Tegretol Oral Suspension	novartis.malta@novartis.com	+356 21222872

Disclaimer
This Direct Healthcare Professional Communication has been submitted to you on behalf of Novartis Ireland Ltd.

The MMA receives the relevant contact details from both the Medical Council and the Pharmacy Council. Should you wish to amend your details including address, you are asked to contact the Medical Council or Pharmacy Council directly, as may apply.