Ref. N°: DD/PVCT/4415 /FDA /2025

SAFETY INFORMATION COMMUNICATION

Medical Product category	Title
Carbamazepine	**Potential risks of born small for gestational age or with microcephaly**

1. Introduction

Reference is made to Law No. 003/20218 of 09/02/2018 establishing Rwanda FDA, and to the regulations governing pharmaceutical products and medical devices, especially Article 23 on safety information and communication.
Referring to the safety information published in WHO Pharmaceuticals Newsletters No.3,205, (1) further reference is also made to the New Zealand Medicines and Medical Devices Safety Authority (Medsafe), which has updated the product information for carbamazepine (Tegretol®) to include the risks of the baby being born small for gestational age or with microcephaly (baby's head is smaller than expected).

2. Description

Carbamazepine is a dibenzapine derivative with antiepileptic and anticonvulsant properties.
Carbamazepine (CBZ) has been extensively used in the treatment of epilepsy, as well as in the treatment of neuropathic pain and affective disorders.

It is also known as Tegretol, an analgesic drug used to control seizures and to treat pain resulting from trigeminal neuralgia. The FDA initially approved it in 1965(2). Interestingly, carbamazepine was the first anticonvulsant used to treat individuals with bipolar disorder(3). It is used as an adjunctive treatment in schizophrenia along with medications and as a second-line agent in bipolar disorder. Carbamazepine appears to work as well as phenytoin and valproate for focal and generalized seizures.

Carbamazepine appears to act by reducing polysynaptic responses and blocking the post-tetanic potentiation. Carbamazepine greatly reduces or abolishes pain induced by stimulation of the infraorbital nerve. The principal metabolite of Carbamazepine-10,11-epoxide has anticonvulsant activity, as demonstrated in several in vivo animal models of seizures (4).

Data from an epidemiological study suggest an increased risk for infants of being born small for gestational age (potentially associated with fetal growth restriction) in pregnant women receiving

antiepileptic drugs (including carbamazepine) during pregnancy compared to unexposed pregnant women with epilepsy(5)(6).

It is in this background that Rwanda FDA warns about the Potential risks of being born small for gestational age or with microcephaly associated with the use of carbamazepine.

3. *Information for the Patients and Caregivers*

- Do not stop taking carbamazepine without talking to your doctor.
- Carbamazepine could harm the way an unborn baby grows and develops during pregnancy.
- Babies born to people who took carbamazepine during pregnancy were found to have increased risks of having a smaller head than expected and being smaller than expected.
- Anyone who could get pregnant should use effective contraception while taking carbamazepine and for two weeks after the last dose.
- Speak with your doctor if you are pregnant or planning to become pregnant while taking carbamazepine.

4. *Information to Healthcare Professionals*

- Congenital malformations and neurodevelopmental disorders have been reported in children following prenatal carbamazepine exposure.
- Carbamazepine should be used during pregnancy only if the potential benefit justifies the potential risks to the foetus.
- Refer people taking carbamazepine who become pregnant for specialist advice.
- People who are planning a pregnancy should switch to an appropriate alternative treatment prior to conception and before contraception is stopped.
- More recently, an observational study found that prenatal carbamazepine exposure was associated with increased risks of being born small for gestational age or with microcephaly in both the overall population and in children born to people with epilepsy.
- For people of childbearing potential, consider performing pregnancy tests before starting carbamazepine and ensure that they are using effective contraception (eg, intrauterine device, medroxyprogesterone injection) during treatment and for two weeks after the last dose.
- Inform people of childbearing potential about the risks of fetal harm if they become pregnant.
- Report all suspected adverse events associated with the use of carbamazepine to the Rwanda FDA.

5. *Information for the Marketing Authorization Holders/Manufacturers*

Rwanda FDA is requesting Marketing Authorization Holders to submit an updated SmPC for Carbamazepine to include Potential risks of born small for gestational age or with microcephaly as an adverse drug reaction. The product label and/or packaging label should also be updated to remind healthcare professionals of the potential effects of Carbamazepine.

6. *Reporting channel*

Patients and Healthcare Professionals are urged to report any suspected adverse drug event/reaction associated with Carbamazepine. or any other medical product to Rwanda FDA by using an online reporting tool called VigiMobile for medicines, which is available on the Rwanda FDA Website at *https://vigiflow-eforms.who-umc.org/rw/adr* or using online reporting system (PViMS) accessible on *https://pvims.rwandafda.gov.rw/security/landing*.

Sincerely,

RWANDA FOOD AND DRUGS AUTHORITY - RWANDA FDA

Prof. Emile BIENVENU
Director General

7. *References*

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4. Summary of Product Characteristics. Encycl Psychopharmacol. 2015;1687–1687.
5. Safety Alert June 2025. 2025;(June):2025.
6. Christensen J, Zoega H, Leinonen MK, Gilhus E, Gissler M, Igland J, et al. Articles Prenatal exposure to antiseizure medications and fetal growth : a population-based cohort study from the Nordic countries. Lancet Reg Heal - Eur [Internet]. 2024;38(February):100849. Available from: https://doi.org/10.1016/j.lanepe.2024.100849