PRAC starts review of topiramate use in pregnancy and women of childbearing potential

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Information on Topiramate

- Topiramate is a medicine used in the EU on its own or together with other medicines to prevent epileptic seizures, prevention of migraine and, in some countries, in combination with phentermine for body weight reduction in fixed-dose combination with phentermine.
- Topiramate is available in the European Union (EU) under various trade names, including Topamax, Topimax, Epitomax, and several generic medicines. In some EU countries topiramate is available in combination with phentermine as Qsiva.

The following products are authorised via national procedures.

Active Ingredients	Product Name	Pharmaceutical Form	Classif-ication	Authorisation Number	MAH/license holder
Topiramate 25mg	Topamax	Film-coated tablets	POM	MA018/00301	Janssen-Cilag International NV
Topiramate 50mg	Topamax	Film-coated tablets	POM	MA018/00302	Janssen-Cilag International NV
Topiramate 100mg	Topamax	Film-coated tablets	POM	MA018/00303	Janssen-Cilag International NV
Topiramate 200mg	Topamax	Film-coated tablets	POM	MA018/00304	Janssen-Cilag International NV
Topiramate 15mg	Topamax	Hard Capsules	POM	MA018/00305	Janssen-Cilag International NV
Topiramate 25mg	Topamax	Hard Capsules	POM	MA018/00306	Janssen-Cilag International NV
Topiramate 50mg	Topamax	Hard Capsules	POM	MA018/00307	Janssen-Cilag International NV
Topiramate 25mg	Topiramate 25mg	Film-coated tablets	POM	MA807/08701	Aurobindo Pharma (Malta) Limited

Topiramate 50mg	Topiramate 50mg	Film-coated tablets	POM	MA807/08702	Aurobindo Pharma (Malta) Limited
Topiramate 100mg	Topiramate 100mg	Film-coated tablets	POM	MA807/08703	Aurobindo Pharma (Malta) Limited
Topiramate 200mg	Topiramate 200mg	Film-coated tablets	POM	MA807/08704	Aurobindo Pharma (Malta) Limited

Information from the EMA about the safety concern

- EMA's safety committee (PRAC) has started a review of topiramate and the risk of neurodevelopmental disorders in children whose mothers were taking topiramate during pregnancy. The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations.

- The review of topiramate has been initiated at the request of the French medicine agency, under Article 31 of Directive 2001/83/EC. This is related to a safety signal review that started in July 2022 and was triggered by a recent study[1] which suggested a possible increase in the risk of neurodevelopmental disorders, in particular autism spectrum disorders and intellectual disability, in children whose mothers were taking topiramate during pregnancy.

- The study was based on data from several Nordic registries (Denmark, Finland, Iceland, Norway, and Sweden), and included information from more than 24,000 children exposed to at least one antiepileptic medicine before birth. Of these children, 471 were exposed to topiramate alone, including 246 children born to mothers who had epilepsy.

- The PRAC started reviewing the study results as part of a safety signal assessment in July 2022. The committee will now conduct an in-depth review of the available data on the benefits and risks of topiramate use in pregnant women and women of childbearing potential in the approved indications. The committee will focus on the current risk minimisation measures and consider the need for additional measures to minimise the risks of topiramate use in these women.

- While the review is ongoing, topiramate should continue to be used according to the authorised product information. Women should discuss any questions or concerns about their topiramate treatment with their doctor or pharmacist. Patients should not stop antiepileptic treatment before speaking with their doctor.

- Following this review, the PRAC will give its recommendation as to whether marketing authorisations of topiramate-containing products should be maintained, varied, suspended, or revoked. These recommendations will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway.

[1] Bjørk M, Zoega H, Leinonen MK, et al. Association of Prenatal Exposure to Antiseizure Medication With Risk of Autism and Intellectual Disability. JAMA Neurol. Published online May 31, 2022. doi:10.1001/jamaneurol.2022.1269.

It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

For more information, please see the European Medicines Agency's press release.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance with topiramate. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 **or** online to http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate

Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

Feedback:

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