HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Topiramate: Introduction of a pregnancy prevention programme and new restrictions on use

The European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) has recommended new measures to avoid exposure to topiramate* during pregnancy in the form of a pregnancy prevention programme (PPP). This follows a review of data suggesting a possible increased risk of neurodevelopmental disorders, including autism spectrum disorders, intellectual disability, and attention deficit hyperactivity disorder (ADHD) following use during pregnancy. The PRAC review also confirmed the known increased risk of major congenital malformation and foetal growth restriction associated with topiramate use during pregnancy[1]. A Direct Healthcare Professional Communication (DHPC)[1] to inform healthcare professionals of the outcome of the review has been distributed in Ireland.

The PRAC has recommended further restrictions on use, including new contraindications for the treatment of epilepsy in pregnancy, unless there is no suitable alternative treatment, and in women of childbearing potential not using highly effective contraception. The only exception is a woman for whom there is no suitable alternative but who plans a pregnancy and who is fully informed about the risks of taking topiramate during pregnancy. Topiramate for prophylaxis of migraine is already contraindicated in pregnancy and in women of childbearing potential not using highly effective contraception.
For women of childbearing potential currently using topiramate, treatment should be re-evaluated to ensure that the measures of the pregnancy prevention programme are followed, key elements of which are described below.

*Products currently authorised that contain topiramate, include, Topamax, and Topamax Sprinkle. Further details are available at www.hpra.ie.

Key elements of the pregnancy prevention programme

In female children and women of childbearing potential:

- Treatment with topiramate should be initiated and supervised by a physician experienced in the management of epilepsy or migraine (use in this indication for women of childbearing potential only).
- Alternative therapeutic options should be considered.
- The need for topiramate treatment in these populations should be reassessed at least annually.

In women of childbearing potential:

- Topiramate for migraine prophylaxis is contraindicated:
  - In pregnancy.
  - In women of childbearing potential not using highly effective contraception.
- Topiramate for epilepsy is contraindicated:
  - In pregnancy, unless there is no suitable alternative treatment.
  - In women of childbearing potential not using highly effective contraception.
  - The only exception is a woman for whom there is no suitable alternative but who plans a pregnancy and who is fully informed about the risks of taking topiramate during pregnancy.

- Pregnancy testing should be performed before initiating treatment.
- The patient must be fully informed and understand the potential risks related to the use of topiramate during pregnancy. This includes the need for a specialist consultation if the woman is planning pregnancy and for prompt contact with a specialist doctor if she becomes pregnant or thinks she may be pregnant.
- At least one highly effective method of contraception (such as an intrauterine device) or two complementary forms of contraception including a barrier method should be used during treatment and for at least 4 weeks after stopping treatment. Due to a potential interaction, women using systemic hormonal contraceptives should be advised to also use a barrier method.
- If a woman is planning to become pregnant, efforts should be made to switch to appropriate alternative epilepsy or migraine treatment before contraception is discontinued. For the treatment of epilepsy, the woman must also be informed about the risks of uncontrolled epilepsy to the pregnancy.
- If a woman being treated with topiramate for epilepsy becomes pregnant, she should promptly be referred to specialists to reassess topiramate treatment and consider alternative treatment options, as well as for careful antenatal monitoring and counselling.
- If a woman being treated with topiramate as migraine prophylaxis becomes pregnant, treatment should be stopped immediately. The woman should be referred to a specialist for careful antenatal monitoring and counselling.

In female children (for epilepsy only):

- Prescribers must ensure that parent(s)/caregiver(s) of female children using topiramate understand the need to contact a specialist once the child experiences menarche.
- At that time, the patient and parent(s)/caregiver(s) should be provided with comprehensive information about the risks due to topiramate exposure in utero, and the need for using highly effective contraception.

Educational Materials

Educational materials for healthcare professionals (HCPs) and patients (female children or their parent(s)/caregiver(s) and women of childbearing potential) will be put in place, including:

- A guide for HCPs.
- A risk awareness form, which must be used and signed at the time of treatment initiation and during each annual review of topiramate treatment by the treating physician.
- A patient guide.
- A patient card, which should be provided each time the medicine is dispensed. The card will be either included inside the package or attached to the outer packaging.

Following HPRA approval, these educational materials will be available on the HPRA website (www.hpra.ie) and will be circulated in hard copy by the marketing authorisation holder for topiramate. A textual warning and a pictogram on the teratogenic risk will be added to the outer packaging of all topiramate-containing medicinal products.

References:

1. Topamax (topiramate) - Important Safety Information from Janssen Sciences Ireland UC as approved by the HPRA (01.11.23), accessible via www.hpra.ie/homepage/medicines/safety-notices