Direct Healthcare Professional Communication

Jan 2024

Topiramate <and topiramate/phentermine combination>:New restrictions to prevent exposure during pregnancy

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following **New restrictions to prevent exposure during pregnancy**

Summary:

- Topiramate can cause major congenital malformations and fetal growth restriction when used during pregnancy. Recent data also suggest a possibly increased risk of neurodevelopmental disorders (NDD) including autism spectrum disorders, intellectual disability and attention deficit hyperactivity disorder (ADHD) following topiramate use during pregnancy.

- For topiramate monocomponent products New contraindications apply for the treatment of epilepsy:
  - 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.
- Topiramate <monocomponent products> for prophylaxis of migraine <and topiramate/phentermine combination products for weight management is/are> already contraindicated in pregnancy and in women of childbearing potential not using highly effective contraception.
- Treatment of female children and women of childbearing potential should be initiated and supervised by a physician experienced in the management of epilepsy or migraine <or weight management for the combination product>.
  The need for treatment should be reassessed at least annually.
- Due to a potential interaction, women using systemic hormonal contraceptives should be advised to also use a barrier method.
- For women of childbearing potential currently using topiramate <or topiramate/phentermine>, the treatment should be re-evaluated to confirm that the pregnancy prevention programme is adhered to.Further information on the safety concern and the recommendations

Background on the safety concern

- Topiramate <monocomponent products is/are> indicated as:
  - Monotherapy in adults, adolescents and children over 6 years of age with partial seizures with or without secondary generalised seizures, and primary generalised tonic-clonic seizures.

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- Adjunctive therapy in children aged 2 years and above, adolescents and adults with partial onset seizures with or without secondary generalisation or primary generalised tonic-clonic seizures and for the treatment of seizures associated with Lennox-Gastaut syndrome.
- Prophylaxis of migraine headache {in adults/in patients 12 years of age and older} after careful evaluation of possible alternative treatment options. Topiramate is not intended for acute treatment.

- Topiramate/phentermine combination products are indicated as:
  An adjunct to reduced calorie diet and physical activity for obese patients (BMI ≥ 30 kg/m2), or overweight patients (BMI ≥ 27 kg/m2) with weight-related co-morbidities such as hypertension, type 2 diabetes or dyslipidaemia.

- Data from two observational population-based registry studies (1, 2) undertaken in largely the same dataset from the Nordic countries suggest that there may be a 2- to3-fold higher prevalence of autism spectrum disorders, intellectual disability or attention deficit hyperactivity disorder (ADHD) in almost 300 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an anti-epileptic drug (AED).
  A third observational cohort study from the U.S.A. did not suggest an increased cumulative incidence of these outcomes by 8 years of age in approximately 1000 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an AED.
  It is already well known that topiramate can cause major congenital malformations and foetal growth restriction when used during pregnancy:

- Infants exposed to topiramate monotherapy in utero have an approximately 3-fold increased risk of major congenital malformations including cleft lip/palate, hypospadias and anomalies involving various body systems compared with a reference group not exposed to antiepileptic drugs. Absolute risks of major congenital malformations following topiramate exposure have been reported in the range of 4.3% (1.4% in the reference group) to 9.5% (3% in the reference group).

- Data from pregnancy registries indicated a higher prevalence of low birth weight (< 2,500 grams) and of being small for gestational age (SGA; defined as birth weight below the 10th percentile corrected for their gestational age, stratified by sex) for topiramate monotherapy. In the North American Antiepileptic Drug Pregnancy Registry, the risk of SGA in children of women receiving topiramate was 18%, compared with 5% in children of women without epilepsy not receiving an AED.

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Reference:

EMA:https://www.ema.europa.eu/en/documents/dhpc/topiramate-and-topiramate-phentermine-combination-new-restrictions-prevent-exposure-during-pregnancy_en.pdf

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: https://primaryreporting.who-umc.org/EG
QR Code:

Hotline: 15301

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