Ipramax®
Topiramate

Physician Guide

Read this Physician Guide carefully before prescribing IPRAMAX® (Topiramate) to women of childbearing potential. This guide aims to minimize pregnancy exposure during treatment with Topiramate.

It provides up-to-date information about the risks of serious congenital malformations, neurodevelopmental disorders, and effects on fetal growth in children of mothers exposed to Topiramate during pregnancy. It also describes the actions necessary to minimize the risks to your patients and ensure your patient has an adequate understanding of the risks.

What are the most important risks I should know about Topiramate use in case of Pregnancy?

- Topiramate can cause major congenital malformations and foetal growth restriction when used during pregnancy. Recent data also suggest a possibly increased risk of neurodevelopmental disorders (NOD) including autism spectrum disorders, intellectual disability and attention deficit hyperactivity disorder (ADHD) following topiramate use during pregnancy.
- 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 for prophylaxis of migraine is 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. 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, the treatment should be evaluated to confirm that the pregnancy prevention program is adhered to.

Background on the safety concern

Topiramate is an anti-epileptic medicine which is used:

- alone to treat seizures in adults and children over age 6,
- with other medicines to treat seizures in adults and children aged 2 years and above,
- to prevent migraine headaches in adults.

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).

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- Data from pregnancy registries indicated a higher prevalence of low birth weight (< 2500 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 as for 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.

For women of childbearing potential currently using topiramate, the treatment should be reevaluated to confirm that the pregnancy prevention program is adhered to (described below).

Key elements of the pregnancy prevention program

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.
- Alternative therapeutic options should be considered.
- The need for topiramate treatment in these populations should be reassessed at least annually.
- Ensure you provide and describe the patient educational and risk minimization materials to the patient (caregivers), which include:
  - Patient Card: Provide a copy or ensure your patient received it. Discuss its contents every time topiramate is dispensed. Advise your patients to keep it with them.
  - Patient Guide: Ensure your patient received it.
  - Form: Complete the Annual Risk Awareness Form with the patient and give them a copy.

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 a pregnancy and for prompt contact with a specialist 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. Women using systemic hormonal contraceptives should be advised to also use a barrier method.

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- If a woman is planning to become pregnant, efforts should be made to switch to an 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 <and migraine> 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.

This medicinal product is subject to additional monitoring. Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pharmacovigilance department in (Tabuk Pharmaceuticals):
Email: pv.info@tabukpharmacuticals.com
Tel: +966114774946

Saudi Food and Drug Authority, National Pharmacovigilance Centre:
Fax: +7662-205-11-966
SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

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This document is approved by the Saudi Food and Drug Authority (SFDA).

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