INCREASED RISK OF ORAL CLEFTS IN INFANTS EXPOSED TO TOPIRAMATE IN UTERO

A recent FDA safety announcement informed the public regarding the increased risk of oral clefts in infants born to women who were treated with Topamax (topiramate) during pregnancy. The verbatim safety announcement can be found below. If you need further information please contact the Samford University Global Drug Information Service at (205) 726-2659.

The U.S. Food and Drug Administration (FDA) is informing the public of new data that show that there is an increased risk for the development of cleft lip and/or cleft palate (oral clefts) in infants born to women treated with Topamax (topiramate) during pregnancy.

The benefits and the risks of topiramate should be carefully weighed when prescribing this drug to women of childbearing age, particularly for conditions not usually associated with permanent injury or death. Alternative medications that have a lower risk of oral clefts and other adverse birth outcomes should be considered for these patients. If the decision is made to use topiramate in women of childbearing age, effective birth control should be used. Oral clefts occur in the first trimester of pregnancy before many women know they are pregnant.

Topiramate was previously classified as a Pregnancy Category C drug, which means that data from animal studies suggested potential fetal risks, but no adequate data from human clinical trials or studies were available at the time of approval. However, because of new human data that show an increased risk for oral clefts, topiramate is being placed in Pregnancy Category D. Pregnancy Category D means there is positive evidence of human fetal risk based on human data but the potential benefits from use of the drug in pregnant women may be acceptable in certain situations despite its risks.

(see Data Summary)

Additional Information for Patients

- If you take topiramate during pregnancy, there is a higher risk that your baby will develop a cleft lip and/or cleft palate. Oral clefts happen early in pregnancy, before many women even know they are pregnant. For this reason, women of childbearing age should talk to their healthcare professionals about other treatment options.
- Women of childbearing age who do decide to take topiramate and are not planning a pregnancy should use effective birth control (contraception) while taking topiramate. Women should talk to their healthcare professionals about the best kind of birth control to use while taking topiramate.
- Before you start topiramate, you should tell your healthcare professional if you are pregnant or are planning to become pregnant. Healthcare professionals may discuss other treatment options with you.
- You should tell your healthcare professional right away if you become pregnant while taking topiramate. You and your healthcare provider should decide if you will continue to take topiramate while you are pregnant.
- Topiramate should not be stopped without talking to a healthcare professional, even in pregnant women. Stopping topiramate suddenly can cause serious problems. Not treating epilepsy during pregnancy can be harmful to women and their developing babies.
- If you become pregnant while taking topiramate, you should talk to your healthcare professional about registering with the North American Antiepileptic Drug Pregnancy Registry. You can enroll in this registry by calling 1-888-233-2334. The purpose of this registry is to collect additional information about the safety of antiepileptic drugs during pregnancy. Information about the North American Drug Pregnancy Registry can be found at http://www.massgeneral.org/aed/.
- Topiramate passes into breast milk, but its effects on developing babies remain unknown. You should talk to your healthcare professional about the best way to feed your baby if you take topiramate.
- You should report any side effects you experience to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of the page.

CONTINUED NEXT PAGE
You should read the Medication Guide when picking up a prescription for topiramate. It will help you understand the potential risks and benefits of this medication.

**Additional Information for Healthcare Professionals**

- You should inform women of childbearing age of the increased risk for oral clefts when topiramate is used in the first trimester of pregnancy.
- You should weigh the benefits and risks of topiramate when prescribing this drug to women of childbearing age, particularly when treating a condition not usually associated with permanent injury or death. Alternative medications that have a lower risk of oral clefts and other adverse birth outcomes should be considered. Healthcare professionals should discuss the relative risks and benefits of appropriate alternative therapies.
- If the decision is made to prescribe topiramate to women of childbearing age, healthcare professionals should recommend use of effective contraception for women who are not planning a pregnancy, keeping in mind the potential for a decrease in hormonal exposure and a possible decrease in contraceptive efficacy when using estrogen-containing birth control with topiramate.
- You should inform patients of the North American Antiepileptic Drug (NAEED) Pregnancy Registry and encourage patients who become pregnant to enroll by calling 1-888-233-2334.
- You should report adverse events involving topiramate to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

**Data Summary**

Data from the North American Antiepileptic Drug (NAAED) Pregnancy Registry indicate an increased risk of oral clefts in infants exposed to topiramate monotherapy during the first trimester of pregnancy. The prevalence of oral clefts was 1.4% compared to a prevalence of 0.38% - 0.55% in infants exposed to other antiepileptic drugs (AEDs), and a prevalence of 0.07% in infants of mothers without epilepsy or treatment with other AEDs. The relative risk of oral clefts in topiramate-exposed pregnancies in the NAAED Pregnancy Registry was 21.3 as compared to the risk in a background population of untreated women (95% Confidence Interval: 7.9 – 57.1). The UK Epilepsy and Pregnancy Register reported a similarly increased prevalence of oral clefts (3.2%) among infants exposed to topiramate monotherapy, a 16-fold increase in risk compared to the risk in their background population (0.2%).

The benefits and the risks of topiramate should be carefully weighed when prescribing this drug for women of childbearing age, particularly when topiramate is considered for a condition not usually associated with permanent injury or death. Appropriate alternative treatment should be considered. Inform women of childbearing age of the increased risk for having a baby with an oral cleft if they become pregnant while using topiramate.

Cleft lip and cleft palate range from a small notch in the lip to a groove that runs into the roof of the mouth and nose, possibly leading to problems with eating, talking and ear infections. Surgery is often used to close the lip and palate. With treatment, most children with cleft lip or palate do well.\(^3\)


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