Data Find High Oral Cleft Risk With Topiramate

BY ELIZABETH MECHCATIE

New data from a national pregnancy registry indicate an increased risk of oral clefts among infants exposed to topiramate monotherapy during the first trimester of pregnancy, which should be considered when prescribing the anticonvulsant to women of childbearing age, the Food and Drug Administration announced.

In the North American Antiepileptic Drugs Pregnancy Registry (NAAED), the prevalence of oral clefts (cleft lip or palate) was 1.4% among infants exposed in utero to topiramate monotherapy during the first trimester, compared with 0.38%-0.55% among infants exposed to other antiepileptic drugs (AEDs).

The rate was 0.07% among infants whose mothers did not have epilepsy or were not treated with other AEDs, according to an FDA statement.

In the NAAED registry, the relative risk of oral clefts among infants exposed to topiramate was 21.3 times that of the background risk among untreated women. The prevalence of oral clefts was also increased among infants exposed to topiramate monotherapy in a U.K. Epilepsy and Pregnancy Register: 3.2% among the infants exposed to topiramate monotherapy, compared with a background prevalence of 0.2% – a 16-fold increase in risk.

"Health care professionals should carefully consider the benefits and risks of topiramate when prescribing it to women of childbearing age," and should consider alternative medications with a lower risk of birth defects, Dr. Russell Katz, director of the division of neurology products in the FDA's Center for Drug Evaluation and Research, said in the FDA statement.

The agency's announcement also notes that if the decision is made to prescribe topiramate to a woman of childbearing age, effective birth control should be used, "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."

The new information is being added to the prescribing information of topiramate, which is also being switched from a pregnancy risk category C (applied to drugs for which animal data suggest potential fetal risks, with no adequate data from human clinical trials or studies) to the pregnancy risk category D (applied to drugs for which there is evidence for human fetal risk based on human data, but potential benefits may be acceptable in certain situations, despite the risks).

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Topiramate, which is marketed as Topamax and is also available in generic formulations, is approved as a treatment for epilepsy and for preventing migraine headaches. ■

Women who are on topiramate and become pregnant should be encouraged to register in the North American AED pregnancy registry by calling 888-233-2334.