5 May 2023

Direct Healthcare Professional Communication

Dear Healthcare Professional,

Janssen in agreement with the Saudi Food and Drug Authority (SFDA), would like to inform you of the recent update to the prescribing information for Topamax® tablets and sprinkle capsules**.** Revisions have been made to the Contraindications, Warnings and Precautions and other relevant information related to the use of topiramate in pregnancy, following the publication of an epidemiological study indicating an increased risk of neurodevelopmental disorders (autism spectrum disorder and intellectual disability) in children exposed to topiramate *in utero*.

It is also intended to remind you about the risks of congenital abnormalities related to the use of topiramate during pregnancy.

Summary

- Topamax can cause fetal harm when administered to a pregnant woman.
- Data from pregnancy registries indicate that infants exposed to topiramate *in utero* have an increased risk of congenital malformations (e.g., craniofacial defects, such as cleft lip/palate, hypospadias, and anomalies involving various body systems) and neurodevelopmental disorders (e.g., autism spectrum disorders and intellectual disability).
- This has been reported with topiramate monotherapy and topiramate as part of a polytherapy regimen.
- Revisions have been made to the Contraindications, Warnings and Precautions and other relevant information related to the use of topiramate in pregnancy to reflect the existing evidence.
- For **migraine prophylaxis**, Topamax is contraindicated in pregnancy and in women of childbearing potential if a highly effective method of contraception is not used.
- For **epilepsy treatment**:
    - Specialist advice should be given to women who are of childbearing potential.

- The need for treatment with antiepileptic drugs (AEDs) should be reviewed when a woman is planning to become pregnant.
- In women being treated for epilepsy, sudden discontinuation of AED therapy should be avoided as this may lead to breakthrough seizures that could have serious consequences for the woman and the unborn child.
- Monotherapy should be preferred whenever possible because therapy with multiple AEDs could be associated with a higher risk of congenital malformations than monotherapy, depending on the associated antiepileptics.

- Topamax should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. In treating and counseling women of childbearing potential, the prescribing physician should weigh the benefits of therapy against the risks and consider alternative therapeutic options. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Additional Information

- An epidemiological study was published on May 31, 2022, in JAMA Neurology (Bjork MH, et al: JAMA Neurol. 2022; 79(7):672-681), investigating the risk of neurodevelopmental disorders in children exposed to antiepileptics in utero. The study reported a 2.77-fold increase in the risk of autism spectrum disorder, and a 3.47-fold increase in the risk of intellectual disability in children with an epileptic mother exposed to topiramate monotherapy during pregnancy, compared to those with epileptic mothers not exposed to antiepileptic treatments during pregnancy.

- Considering this new information, the Prescribing Information for Topamax® tablets and sprinkle capsules was updated as following:

  - **Contraindications:**

  - **New contraindication:** Migraine prophylaxis in pregnancy and in women of childbearing potential if not using a highly effective method of contraception.

  - **Warning and Precautions – Women of Childbearing Potential:**

  - **New recommendation:** Before the initiation of treatment with topiramate in a woman of childbearing potential, pregnancy testing should be performed and a highly effective contraceptive method used. The patient should be fully informed of the risks related to the use of topiramate during pregnancy.

  - **Pregnancy and Breast Feeding:**

  - Added text reporting the increased risk of neurodevelopmental disorders (e.g. autism spectrum disorders and intellectual disability) in infants exposed to topiramate in utero:

- Topamax can cause fetal harm when administered to a pregnant woman. Data from pregnancy registries indicate that infants exposed to topiramate in utero have an increased risk of congenital malformations (e.g., craniofacial defects, such as cleft lip/palate, hypospadias, and anomalies involving various body systems) and neurodevelopmental disorders (e.g., autism spectrum disorders and intellectual disability).

- Added recommendations in **epilepsy**:

  - Consider alternative therapeutic options in women of childbearing potential.
  - If Topamax is used in women of childbearing potential, it is recommended that highly effective contraception be used and that the woman is fully informed of the known risks of uncontrolled epilepsy to the pregnancy and the potential risks of the medicinal product to the fetus.
  - If a woman plans a pregnancy, a preconceptional visit is recommended in order to reassess the treatment, and to consider other therapeutic options.
  - In case of administration during the first trimester, careful prenatal monitoring should be performed.

- Added text about the **risk related to epilepsy and AEDs in general**:
  - Specialist advice should be given to women who are of childbearing potential.
  - The need for treatment with AEDs should be reviewed when a woman is planning to become pregnant.
  - In women being treated for epilepsy, sudden discontinuation of AED therapy should be avoided as this may lead to breakthrough seizures that could have serious consequences for the woman and the unborn child.
  - Monotherapy should be preferred whenever possible because therapy with multiple AEDs could be associated with a higher risk of congenital malformations than monotherapy, depending on the associated antiepileptics.

The information in this letter has been approved by the Saudi Food and Drug Authority (SFDA).

Please refer to the Prescribing Information for Topamax® tablets and sprinkle capsules for additional information.

Call for reporting

Healthcare professional should report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system:

SFDA (National Pharmacovigilance Center):
Email : npc.drug@sfda.gov.sa
Telephone : 19999
Online: http://ade.sfda.gov.sa

Company Contact Points:
If you have further question or require additional information, please contact our local safety department at:

Email: GCC-PV2@its.jnj.com
Tel: +966 11 4339133

Yours sincerely,

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