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6 April 2023

PREGNANCY RELATED SAFETY UPDATE FOR TOPAMAX® (TOPIRAMATE) TABLETS AND SPRINKLE CAPSULES. UPDATED INFORMATION AND REMINDER ON:

- **CONTRAINDICATIONS**
- **WARNINGS AND PRECAUTIONS**
- **USAGE OF TOPIRAMATE IN PREGNANCY AND BREAST FEEDING**

Dear Healthcare Professional,

Janssen-Cilag (New Zealand) Ltd ('Janssen'), in consultation with MEDSAFE, would like to inform you about the following safety updates to the Data Sheet for TOPAMAX® (topiramate) TABLETS (25 mg, 50 mg, 100 mg & 200 mg) and SPRINKLE CAPSULES (15 mg, 25 mg & 50 mg).

Revisions have been made to the section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE and section 4.6 FERTILITY, PREGNANCY AND LACTATION related to the use of topiramate in pregnancy.

This follows 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*.

This letter intends 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)
- Data from an epidemiological study indicates in uterus exposure to topiramate can lead to an increased risk of 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 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 all 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. All women of childbearing potential should use a highly effective method of contraception.
    - 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 in the data sheet for Topamax® tablets and sprinkle capsules was updated with the following:

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- **Section 4.4: Special 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.

- For migraine prophylaxis, TOPAMAX® is contraindicated in pregnancy and in women of childbearing potential if a highly effective method of contraception is not used. TOPAMAX® should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

- **Section 4.6: Fertility, Pregnancy and Lactation:**

- 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 text about the **risk related to epilepsy and AEDs in general**:

  - 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.

Please refer to the Data Sheet for Topamax® tablets (25 mg, 50 mg, 100 mg & 200 mg) and sprinkle capsules (15 mg, 25 mg & 50 mg) for additional information.

Adverse Event Reporting:
Janssen is committed to monitoring the safety of our products. We encourage healthcare professionals to report any suspected adverse events for TOPAMAX® to to the Centre for Adverse Reactions Monitoring via either their online reporting form, available at https://nzphvc.otago.ac.nz/report/, by phone on 03 479 7247 or by email at carmnz@otago.ac.nz and/or Janssen's Medical information Department.

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Company Contact Point:
For additional information regarding TOPAMAX®, please refer to the Product Datasheet (https://www.janssen.com/newzealand/sites/www_janssen_com_newzealand/files/prod_files/live/topamax_data_sheet.pdf) or contact Janssen Medical Information on 0800 800 806 or medinfo@janau.jnj.com for additional support.

Yours sincerely,

Sophie Glover-Koudounas

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