

Important Safety Information on Topiramate (TOPAMAX)

Healthcare professional guide

Topiramate (TOPAMAX) monocomponent products

Healthcare professional guide including a risk awareness form

Guide for healthcare professionals who manage female children and women of childbearing potential treated with topiramate

Guide on topiramate pregnancy prevention program

This risk minimization document has been reviewed and approved by the Saudi Food and Drug Authority (SFDA), Oct 2024, Version 1

What are the risks of topiramate if taken during pregnancy?

Topiramate is teratogenic. Children exposed in utero to topiramate have a higher risk for congenital malformations, low birth weight and being small for gestational age (SGA).

There may also be an increased risk for neurodevelopmental disorders.

Congenital malformations

- In the North American Antiepileptic Drug Pregnancy Registry about 4.3% of children exposed to topiramate monotherapy had a major congenital malformation compared to 1.4% in a reference group not taking antiepileptic drugs (AEDs).
- The most common types of malformation included: cleft lip and cleft palate, hypospadias and anomalies involving various body systems.
- A population-based registry study from the Nordic countries also showed a 2- to 3-fold higher prevalence of major congenital malformations (up to 9.5%), compared with a reference group not taking AEDs (3.0%).
- Studies indicate that, compared with monotherapy, there is an increased risk of teratogenic effects associated with the use of AEDs in combination therapy. The risk has been reported to be dose dependent; adverse effects were observed even with low doses.

Fetal growth restriction

- A higher prevalence of low birth weight (<2500 grams) and of being SGA (defined as birth weight below the 10th percentile corrected for their gestational age, stratified by sex) was found in topiramate-exposed children compared with a reference group. In the North American Antiepileptic Drug Pregnancy Registry, the risk of SGA in children of women receiving topiramate was 18%, compared with 5% for women without epilepsy not receiving an AED.

Neurodevelopmental disorders

- Data from two observational population-based registry studies undertaken in largely the same dataset from the Nordic countries suggest that there may be a 2- to 3-fold higher prevalence of autism spectrum disorders, intellectual disability or ADHD in almost 300 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an AED in utero.
- A third observational cohort study from the U.S.A. did not suggest an increased prevalence of these outcomes in approximately 1000 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an AED in utero.

What you must know about the conditions of topiramate prescription in female patients

Pregnancy prevention programme

- Topiramate is **contraindicated** in the following conditions:

Prophylaxis of migraine

- in pregnancy.
- in women of childbearing potential not using highly effective contraception.

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.

- Treatment with topiramate should be initiated and **supervised by physicians experienced** in the management of epilepsy or migraine.
- Ensure that your **patient is fully informed and aware of the potential risks related to topiramate use during pregnancy.**
- **Fully inform** your patient with epilepsy **about** the **risks of untreated epilepsy** to her and the unborn child.
- **Consider other treatment options** in female children and women of childbearing potential **in all indications**.
- The need for topiramate **treatment** in these populations **should be reassessed at least annually**. (See box at the end of this guide).
- Advise the patient to **promptly contact you if** she has become **pregnant** or thinks she might be pregnant.

Female children

- Make every effort to **switch female children** to alternative treatment **before** they reach **menarche**.
- **Explain the risks** due to topiramate use during pregnancy **to the parents**/ caregivers (and their children depending on their age).
- **Explain** the **importance of contacting you once** a **female child experiences menarche** and about the need to use **highly** effective contraception as soon as it is relevant.

Contraception

- Perform a **pregnancy test** prior to treatment initiation.
- Counsel on the need for highly **effective contraception** throughout the treatment and 4 weeks after treatment discontinuation. Guidance on contraceptive methods should be provided, preferably in collaboration with a specialist (e.g. gynaecologist).

What you must know about the conditions of topiramate prescription in female patients (Cont'd)

- 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.
- Inform your patient about the possibility of decreased contraceptive efficacy if taking **systemic hormonal contraceptive products** with topiramate. Women using **systemic** hormonal contraceptives should **add a barrier method**.



Pregnancy planning

- Explain the need for **pregnancy planning**.
- **Reassess topiramate treatment**. If possible, **switch** to alternative treatment **before contraception is discontinued**.
- Explain that **switch** to alternative treatment in epilepsy **takes time**, as the new treatment might be gradually introduced as add-on to topiramate and then topiramate is gradually withdrawn.
- Advise the patient to **promptly contact you if** she has become **pregnant** or thinks she might be pregnant.



If your patient has become pregnant while treated with topiramate

- **In** patients with **migraine stop treatment** with topiramate.
- **In** patients with **epilepsy reassess topiramate treatment**. Consider alternative treatment options or promptly refer your patient to a specialist for reassessment. Inform your patient to keep taking her treatment until her next consultation due to the **risk of breakthrough seizures** having serious consequences for the woman and the unborn child.
- Ensure that your patient is **fully informed about and understands the risks** of topiramate during pregnancy using the Risk Awareness Form.
- If topiramate has been or is used during pregnancy, careful **prenatal monitoring** should be performed.
- During pregnancy topiramate should preferably be prescribed:
  - as monotherapy,
  - at the lowest effective dose.

- (Re-)Assess the need for topiramate therapy by completing the Risk Awareness Form with the patient at initiation, annual review, when your patient plans a pregnancy or has become pregnant.
- Provide the **Patient Guide**.

This risk minimization document has been reviewed and approved by the Saudi Food and Drug Authority (SFDA)

Risk Awareness Form

for female children and women who are able to become pregnant while treated with topiramate

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Risk Awareness Form for female children and women who are able to become pregnant while treated with topiramate

Part A- To be completed <and signed> by the treating physician

- This form is intended to facilitate the annual reassessment of your female patients, to make sure that female patients or their caregiver(s) </legal representative(s)> have been fully informed about and understand the risks related to the use of topiramate during pregnancy.
- Complete the Risk Awareness Form with your patient at initiation, at annual review, when your patient plans a pregnancy or has become pregnant.
- This form should be used together with the healthcare professional guide, which contains detailed information.
- A copy of this form completed <and signed> shall be kept / recorded by the physician.

Name and ID of patient (if appropriate also name of caregiver</legal representative>):

_____

The need for topiramate treatment has been evaluated for the above-named patient.
The following points have been discussed with the patient and/or parent/caregiver </legal representative>:

Risks to children exposed to topiramate during pregnancy	☐
(If applicable:) Risk of untreated epilepsy to mother and to an unborn child	☐
Pregnancy test before treatment initiation (if the patient has already reached menarche)	☐
Need for regular (at least annually) review by a specialist	☐
Need for **highly** effective contraception during treatment and 4 weeks after discontinuation	☐
Importance of pregnancy planning	☐
Importance of contacting physician in case of (suspected) pregnancy	☐
Provision of patient guide	☐

In case of pregnancy:

Need for prenatal monitoring of the child	☐
Evaluation of alternative treatment or treatment change	☐
When used for epilepsy: Evaluation of alternative treatment or treatment change	☐
When used to prevent migraine: Importance of immediately stopping treatment	☐

Name of physician _____ Signature _____ Date _____

Part B- To be completed <and signed> by the patient or caregiver </legal representative>

Read and complete this form during a visit with your doctor: at treatment start, at the annual visit, when you are planning a pregnancy or if you are pregnant.

This is to make sure that you have discussed with your doctor and understand the risks related to the use of topiramate during pregnancy.

Keep a copy of this form completed and signed.

I have discussed the following points with my doctor:

Why I need topiramate rather than another medicine	☐
That **children** whose mothers took topiramate during pregnancy: • have a **higher risk** of birth defects, • have a **higher risk** of being smaller and weighing less than expected at birth, • may have a **higher risk** of developmental problems	☐
(If you take topiramate for epilepsy:) That **untreated epilepsy** can also put me and my unborn child at risk	☐
Why I need a **negative pregnancy test** before treatment with topiramate is started	☐
That I must **use highly effective contraception** without interruption during the entire duration of my treatment with topiramate and for 4 weeks after stopping treatment	☐
(If applicable:) That the doctor is informed as soon as I **experience my first period** during treatment with topiramate	☐
That I should **visit a doctor regularly** (at least annually) to review whether topiramate remains the best treatment option for me	☐
The need to **consult my doctor** if I plan to become pregnant, to evaluate if it is possible to switch to alternative treatment before I stop my contraception	☐
That I should **promptly talk to my doctor if** I think I am **pregnant**	☐
I have received a copy of the patient guide	☐
In case of pregnancy: That I need appropriate monitoring of my unborn child	☐

Name of patient/caregiver </legal representative> Signature Date

ADVERSE EVENTS REPORTING GUIDANCE

SFDA (National Pharmacovigilance center)

Email: npc.drug@sfda.gov.sa

Telephone: 19999

Online: http://ade.sfda.gov.sa

For full prescribing information, please refer to the datasheet or contact Johnson & Johnson Trading Limited (Riyadh)

Address: Prince Muhammed Bin Abdulaziz Rd, Tower B, Level 30, Olaya towers. Postal address: P O Box 65305 Riyadh 11556, Saudi Arabia, Office Tel 00966-11-4339133

To report Adverse Events/Product Complaint or any Medical Information Inquiries, please contact us at:

Email: GCC-PV2@its.jnj.com, Hotline: 00966540015811

ADHD, attention deficit hyperactivity disorder; AEDs, antiepileptic drugs; SGA, small for gestational age; WCBP, Women of Childbearing Potential.

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