



Healthcare professional guide

Topiramate 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 programme

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 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 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.

{To be agreed at a national level:

A link to the dedicated website, indicating to patients where additional online information about topiramate use in WCBP can be found.}

- (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**.

Risk Awareness Form

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

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

{signing subject to national implementation}

- 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.

{signing and recording subject to national implementation}.

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	<input type="checkbox"/>
(If applicable:) Risk of untreated epilepsy to mother and to an unborn child	<input type="checkbox"/>
Pregnancy test before treatment initiation (if the patient has already reached menarche)	<input type="checkbox"/>
Need for regular (at least annually) review by a specialist	<input type="checkbox"/>
Need for highly effective contraception during treatment and 4 weeks after discontinuation	<input type="checkbox"/>
Importance of pregnancy planning	<input type="checkbox"/>
Importance of contacting physician in case of (suspected) pregnancy	<input type="checkbox"/>
Provision of patient guide	<input type="checkbox"/>

In case of pregnancy:

Need for prenatal monitoring of the child	<input type="checkbox"/>
Evaluation of alternative treatment or treatment change	<input type="checkbox"/>
When used for epilepsy: Evaluation of alternative treatment or treatment change	<input type="checkbox"/>
When used to prevent migraine: Importance of immediately stopping treatment	<input type="checkbox"/>

Name of physician

Signature

Date

Part B- To be completed <and signed> by the patient or caregiver </legal representative>
{signing subject to national implementation}

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	<input type="checkbox"/>
That children whose mothers took topiramate during pregnancy: <ul style="list-style-type: none">• 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	<input type="checkbox"/>
(If you take topiramate for epilepsy:) That untreated epilepsy can also put me and my unborn child at risk	<input type="checkbox"/>
Why I need a negative pregnancy test before treatment with topiramate is started	<input type="checkbox"/>
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	<input type="checkbox"/>
(If applicable:) That the doctor is informed as soon as I experience my first period during treatment with topiramate	<input type="checkbox"/>
That I should visit a doctor regularly (at least annually) to review whether topiramate remains the best treatment option for me	<input type="checkbox"/>
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	<input type="checkbox"/>
That I should promptly talk to my doctor if I think I am pregnant	<input type="checkbox"/>
I have received a copy of the patient guide	<input type="checkbox"/>
In case of pregnancy: That I need appropriate monitoring of my unborn child	<input type="checkbox"/>

Name of patient/caregiver </legal representative>

Signature

Date

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: <https://primaryreporting.who-umc.org/EG>

QR Code:



Hotline: 15301

Company contact points :

Janssen scientific office:

Address: Building 44, North Teseen street, 5th settlement, New Cairo, P.O Box 11835, Cairo, Egypt

Telephone: +2 21291100

Mobile: +2 01000629760

E-mail: JACEG-PV@its.jnj.com



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



Patient guide

What females who are able to become pregnant need to know about topiramate

Please keep this booklet. You may need to read it again.

What are the risks of taking topiramate during pregnancy?

- **Topiramate can seriously harm an unborn child** when taken during pregnancy.
- However, if you are taking topiramate for epilepsy you should never stop taking it unless your doctor tells you so because your epilepsy may become worse, which may also put you and your unborn child at risk.
- If you take **topiramate** during pregnancy, your child has a **threefold higher risk for birth defects**, particularly
 - Cleft lip (split in the top lip) and cleft palate (split in the roof of the mouth).
 - Newborn boys may also have a malformation of the penis (hypospadias).

These defects can develop early in pregnancy, even before you know you are pregnant.

- If you take topiramate during pregnancy, your **child may be smaller and weigh less** than expected at birth. In one study, 18 % of children of mothers taking topiramate during pregnancy were smaller and weighed less than expected at birth, while 5 % of children born to women without epilepsy and not taking antiepileptic medication were smaller and weighed less than expected at birth.

What are the risks of taking topiramate during pregnancy? (Cont'd)

- If you take topiramate during pregnancy, your child may have a 2- to 3-fold higher risk for autism spectrum disorders, intellectual disabilities, or attention deficit hyperactivity disorder (ADHD) compared with children born to women with epilepsy not taking antiepileptic medication.

What you should remember when taking topiramate



Need for contraception

- **Always use highly effective contraception** recommended by your doctor or gynaecologist for the whole time you are taking topiramate and for four weeks after stopping treatment.
- This is to prevent you getting pregnant on topiramate since it can harm your unborn child.
- Talk to your doctor about the method of birth control (contraception) that is most appropriate for you.
- If you are taking hormonal contraceptives, there is the risk for reduced effectiveness of hormonal contraceptives due to topiramate. Therefore, an additional barrier contraceptive method such as a condom or pessary/diaphragm should be used.
- Tell your doctor if your menstrual bleeding changes.



Use in girls {for epilepsy only}

For a girl who has **not yet experienced her first periods**:

- You/the parent or caregiver should know about the risks of topiramate when used during pregnancy, as this will be important when you/the child gets older.
- Inform the doctor as soon as the **girl experiences her first periods** during topiramate treatment.
- **As soon as you are sexually active, you need to use highly effective contraception.** It is very important that you talk to your parents and your doctor about that. Your doctor or gynaecologist will counsel about which method of contraception is best for you.

What you should remember when taking topiramate (Cont'd)

If you already **have your periods**:

- In case you are sexually active, you should only be treated with topiramate if you are not pregnant and you are using **highly** effective contraception.



If you wish to become pregnant while taking topiramate

- Schedule an appointment with your doctor. It is important that you do not stop using contraception (birth control) and do not become pregnant until you have discussed your options with your doctor.
- Your doctor will reassess your treatment and evaluate alternative treatment options. The doctor will counsel you about the risks of topiramate during pregnancy. He/she may also refer you to another specialist.



If you have become pregnant or think you may be pregnant while taking topiramate

- If you are taking topiramate for **epilepsy**, do not stop taking this medicine until you have discussed this with your doctor, as this may worsen your illness. Worsening of your epilepsy may put you or your unborn child at risk.
- If you are taking topiramate to **prevent migraine**, stop taking the medicine straight away, and contact your doctor to evaluate if you need alternative treatment.
- Your doctor will reassess your treatment and evaluate alternative treatment options. The doctor will counsel you about the risks of topiramate during pregnancy.
- **Talk promptly to your doctor** about your options and what you need to know.
- Your doctor will explain if you need to switch to another treatment and how.
- If treatment with topiramate is continued, make sure you are referred to a specialist for prenatal monitoring to check how your child is developing.

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Mobile: +2 01000629760

E-mail: JACEG-PV@its.jnj.com



Consult your doctor regularly – at least each year. During this visit you will read <and sign> a Risk Awareness Form together with your doctor to ensure you know and understand the risks related to topiramate use during pregnancy and the need to use highly effective contraception. This visit is also to check the need for your topiramate treatment and to consider alternative treatment options.