

**PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) – 1986**

The medicine is dispensed with a doctor's prescription only

Name of the preparation and its form:

Topamax® 25

Topamax® 50

Film-coated tablets

The active ingredient and its quantity:

Each tablet contains:

Topiramate 25 mg

Each tablet contains:

Topiramate 50 mg

Topamax® 100

Topamax® 200

Film-coated tablets

The active ingredient and its quantity:

Each tablet contains:

Topiramate 100 mg

Each tablet contains:

Topiramate 200 mg

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

This medicine is not intended for infants and children under 2 years of age or as monotherapy under 7 years of age.

Patient Safety Information Card

In addition to the leaflet, Topamax has a Patient Safety Information Card.

This card includes important safety information, which you should know before beginning and during treatment with Topamax, and act accordingly. Read the Patient Safety Information Card and the patient leaflet before beginning to use the preparation. Keep the card and the leaflet for further reference if needed.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended for:

- Treatment of seizures. For use in combination with other medicines in adults and children from 2 years of age and above, or as monotherapy in adult patients and in children aged 7 years and above.
- Prevention of migraine in adults. The preparation is not intended for alleviating pain during a migraine attack.

Therapeutic group: Antiepileptics

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

(X) You are sensitive to the active ingredient or to any of the additional ingredients contained in the medicine, listed in section 6.

Migraine prevention

(X) Do not use Topamax if you are pregnant.

(X) If you are a woman who is able to become pregnant, do not use Topamax unless you are using highly effective contraceptives during the course of treatment with Topamax (further information in the section 'Pregnancy and breastfeeding – Important advice for women who are able to become pregnant').

Treatment of epilepsy

(X) Do not use Topamax if you are pregnant, unless no other treatment provides sufficient seizure control.

(X) If you are a woman who is able to become pregnant, you must not use Topamax unless you are using highly effective contraceptives during the course of treatment with Topamax. The only exception is if Topamax is the only treatment that provides sufficient seizure control and you are planning to become pregnant. Speak to the doctor to make sure you have received information about the risks of taking Topamax during pregnancy and the risks of seizures during pregnancy (further information in section 'Pregnancy and breastfeeding – Important advice for women who are able to become pregnant').

Special warnings regarding use of the medicine

- **Do not use the medicine without consulting the doctor before commencing treatment if:**

- You suffer from kidney problems, especially kidney stones, or you are a patient being treated with dialysis
- You have a history of problems related to blood and body fluids (metabolic acidosis)
- You suffer from liver problems
- You suffer from eye problems (especially glaucoma)
- You suffer from growth problems
- You are on a ketogenic diet (a low-carbohydrate, high-fat diet)
- You are woman who is able to become pregnant. Topamax may harm an unborn child when taken during pregnancy. Highly effective contraceptives must be used during the course of treatment with Topamax and for at least 4 weeks from the end of the Topamax treatment (see 'Pregnancy and breastfeeding' section for further information)

- You are pregnant. Topamax may harm an unborn child when taken during pregnancy.

If any of the conditions above apply to you, speak with the doctor before using the medicine.

- If you have epilepsy, it is important that you do not stop taking the medicine without first consulting the doctor.
- Do not take any other medicine containing topiramate, given to you as a substitute for this medicine, without first consulting the doctor.
- You may lose weight while using Topamax. Weigh yourself regularly during the course of treatment with Topamax. If you lose a lot of weight or if a child being treated with Topamax does not gain enough weight, consult the doctor.
- In a small number of patients treated with antiepileptics such as Topamax, suicidal thoughts or suicidal behavior have been reported. In case suicidal thoughts occur, refer to the doctor immediately!
- Topamax can cause serious skin side effects. Tell your doctor immediately if you develop a skin rash and/or blisters.
- Topamax may in rare cases cause high levels of ammonia in the blood (seen in blood tests) which can lead to a change in brain function, mainly when given in combination with valproic acid or sodium valproate. Since this may be a severe condition, refer to the doctor immediately if the following symptoms occur:
 - Difficulty thinking, remembering information, or solving problems
 - Sensation of less alertness/vigilance
 - Feeling of sleepiness and a lack of energy

At high doses of Topamax, the risk of developing these symptoms may increase.

Children and adolescents

The side effects in children are generally similar to those in adults. However, the side effects specified in the section 'Side effects in children' may be more common in children than in adults.

Tests and follow-up

A pregnancy test should be performed before starting treatment with Topamax.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Topamax and other medicines can affect each other. The doctor will consider whether the dosage of Topamax or of your other medicines needs to be adjusted.

In particular, inform the doctor or pharmacist if you are taking:

- Other medicines that affect or decrease your level of thinking,

concentration or muscle coordination (e.g., central nervous system depressants such as muscle relaxants and sedative and sleep medicines).

- Hormonal contraceptives. Topamax may make hormonal contraceptives less effective. An additional barrier method of contraception such as a condom or pessary (intrauterine device)/diaphragm should be used. Talk to your doctor about the most suitable type of contraception to use during treatment with Topamax.

Tell the doctor if your menstrual bleeding changes while using hormonal contraceptives and Topamax. Irregular bleeding may occur. In such cases – continue taking the hormonal contraceptive and inform the doctor.

Make a list of all the medicines you are taking and show this list to your doctor or pharmacist each time before you start taking a new medicine.

The following medicines should also be discussed with your doctor or pharmacist:

- Other antiepileptics
- Risperidone (for the treatment of schizophrenia)
- Lithium (for the treatment of manic depression)
- Hydrochlorothiazide, propranolol, diltiazem (for the treatment of heart problems and to lower blood pressure)
- Metformin, pioglitazone, glibenclamide (for the treatment of diabetes)
- Amitriptyline, venlafaxine (for the treatment of depression)
- Flunarizine (for the prevention of migraines and for the treatment of vertigo)
- *Hypericum perforatum* (St. John's wort – a herbal medicine to treat depression)
- Warfarin for thinning the blood

Use of the medicine and food

Topamax may be taken with or without food.

Be sure to drink plenty of fluids during the course of treatment (to reduce the risk of formation of kidney stones).

Use of the medicine and alcohol consumption

Abstain from drinking alcohol during the course of treatment with the medicine.

Pregnancy and breastfeeding

Important advice for women who are able to become pregnant

Topamax may harm an unborn child. If you are a woman who is able to become pregnant, talk to the doctor about alternative treatment options. Visit your doctor to review your treatment and discuss the risks at least once a year.

Migraine prevention

For migraine, you must not use Topamax if you are pregnant.

For migraine, you must not use Topamax if you are a woman who is able to become pregnant unless you are using highly effective contraception.

Before the start of treatment with Topamax, a pregnancy test should be performed in a woman who is able to become pregnant.

Treatment of epilepsy

For epilepsy, you must not use Topamax if you are pregnant, unless no other treatment gives sufficient seizure control for you.

For epilepsy, you must not use Topamax if you are a woman who is able to become pregnant unless you are using highly effective contraception. The only exception is if Topamax is the only treatment providing sufficient seizure control, and you are planning to become pregnant.

Speak to the doctor to make sure you have received information about the risks of taking Topamax during pregnancy, and about the risks of seizures during pregnancy that may put the unborn child at risk.

Before starting treatment with Topamax, a pregnancy test should be performed in a woman who is able to become pregnant.

The risks of topiramate when taken during pregnancy (irrespective of the indication for which it is given):

There is a risk of harm to the unborn child if Topamax is used during pregnancy. If you are taking Topamax during pregnancy, there is an increased risk for birth defects. In women who take Topamax, 4-9 children in every 100 will have birth defects. This compares to 1-3 children in every 100 born to women who do not have epilepsy and are not taking antiepileptics. Particularly, cleft lip (a split in the top lip) and cleft palate (a split in the roof of the mouth) have been observed. Newborn boys may have a malformation of the penis (hypospadias). These defects can develop in early stages of pregnancy, sometimes before the pregnancy is detected.

If you take Topamax during pregnancy, there is a 2-3-fold higher risk for autism spectrum disorders, intellectual disabilities, or attention deficit hyperactivity disorder (ADHD) compared to children born to women with epilepsy not taking antiepileptics.

When taking Topamax during pregnancy, your child may be smaller and weigh less than expected at birth. In one study, 18% of children of mothers taking Topamax during pregnancy were smaller and weighed less than expected at birth, while 5% of the children born to mothers without epilepsy and not taking antiepileptics were born small and weighed less than expected at birth.

- Consult the doctor if you have questions about this risk during pregnancy.
- There may be other medicines to treat your condition that have a lower risk of birth defects.

Need for contraception in women who are able to become pregnant

If you are a woman who is able to become pregnant, talk to the doctor about alternative treatments instead of Topamax. If the decision was made to use

Topamax, use a highly effective contraceptive during the course of treatment and for 4 weeks after the end of treatment.

Use one highly effective contraceptive (such as an intrauterine device) or two complementary contraceptives such as birth control pills together with a barrier method of birth control (such as a condom or pessary (intrauterine device)/diaphragm). Consult the doctor about which contraceptive is most appropriate for you.

If you are taking hormonal contraceptives, there is the possibility of reduced effectiveness of the contraceptive when used with Topamax. Therefore, an additional barrier contraceptive method (such as a condom, pessary (intrauterine device), or diaphragm) should be used.

Tell the doctor if you experience irregular menstrual bleeding.

Use of Topamax in girls

If you are a parent or a caregiver of a girl treated with Topamax, contact the attending doctor once she gets her first period. The doctor will inform you of the risks to an unborn child due to Topamax exposure during pregnancy, and of the need for using highly effective contraception.

If you wish to become pregnant during the course of treatment with Topamax

- Schedule an appointment with the attending doctor.
- Do not stop using the contraceptive before talking to your doctor.
- If you are taking Topamax for epilepsy, do not stop taking it until you talk to your doctor, because your illness may become worse.
- The doctor will reassess the treatment and evaluate alternative treatment options. The doctor will counsel you about the risks of Topamax during pregnancy. He/she may refer you to another specialist.

If you have become pregnant or think you are pregnant while taking Topamax

- Schedule an urgent appointment with the doctor.
- If you are taking Topamax to prevent migraine, stop taking the medicine immediately, and contact the doctor to evaluate if you need alternative treatment.
- If you are taking Topamax for epilepsy, do not stop taking this medicine until you talk to your doctor, as it may worsen your illness. Worsening of your epilepsy may put you or your unborn child at risk.
- The doctor will reassess the treatment and consider alternative treatments. The doctor will counsel you about the risks of taking Topamax during pregnancy. He/she may refer you to another specialist.

If Topamax is taken during pregnancy, check-ups should be conducted frequently to assess how the unborn child is developing.

Breastfeeding

The active ingredient in Topamax (topiramate) passes into breast milk. Effects have been seen in breastfed babies of mothers treated with Topamax, including diarrhea, sleepiness, irritability, and poor weight gain.

Therefore, the doctor will discuss with you whether to abstain from breastfeeding or to abstain from treatment with Topamax. The doctor will weigh the importance of the medicine to the mother versus the risk to the baby.

Mothers who breastfeed while taking Topamax should tell the doctor immediately of any unusual effect experienced by the baby.

Driving and operating machinery

Use of the medicine may cause dizziness, tiredness and vision problems.

Do not drive or use tools or machines without talking with the doctor first.

Important information about some of the ingredients of the medicine

Topamax tablets contain lactose.

If you have an intolerance to certain sugars, consult with the doctor before using the medicine.

Topamax tablets contain less than 1 mmol sodium (23 mg) per tablet, which is considered to be essentially "sodium-free".

3. HOW SHOULD THE MEDICINE BE USED?

Always use the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

The doctor will usually start with a low dosage of Topamax and slowly increase the dosage until the dosage suitable for you is found.

Do not exceed the recommended dosage.

Method of administration – Swallow Topamax tablets whole. Avoid chewing the tablet as it may leave a bitter taste.

- Topamax can be taken before, with or after food.
- Be sure to drink a lot during the day to prevent the formation of kidney stones during treatment.

Girls and women who are able to become pregnant

Topamax treatment should be started and supervised by a doctor specializing in the treatment of epilepsy or migraine. Consider alternative treatments for girls and women of child-bearing potential. Visit your doctor at least once a year to review your treatment.

If you accidentally take too high a dose

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you. Do not induce vomiting unless explicitly instructed to do so by the doctor!

If you took an overdose, you may feel sleepy, tired or less alert, experience a lack of coordination, difficulty speaking or difficulty concentrating, double

vision or blurred vision, a feeling of depression or irritability, dizziness due to low blood pressure, abdominal pain, seizures.

Overdose can occur when you take other medicines together with Topamax.

If you forget to take this medicine, take a dose as soon as you remember, but if you remember close to the time for taking the next dose, skip the forgotten dose and continue as usual. Do not under any circumstances take two doses together!

If you miss two or more doses, contact the doctor.

If you stop taking the medicine

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment without consulting the doctor, as the symptoms may return. If the doctor decides to discontinue treatment, the dosage will be decreased gradually over a few days.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Topamax may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Refer to the doctor immediately if you notice any of the following effects:

Very common side effects – effects that occur in more than 1 user in 10

Depression (new or worsening)

Common side effects – effects that occur in 1-10 in 100 users

- Seizures
- Anxiety, irritability, changes in mood, confusion, disorientation
- Concentration disturbances, slowed thinking, loss of memory, problems with memory (new onset, sudden change or deterioration)
- Kidney stones, frequent or painful urination

Uncommon side effects – effects that occur in 1-10 in 1,000 users

- Increased acid level in the blood (may cause breathing problems including shortness of breath, loss of appetite, nausea, vomiting, excessive tiredness, and fast or uneven heartbeats)
- Decreased or termination of sweating (particularly in young children who are exposed to high temperatures)
- Thoughts and attempts of serious self-harm

- Loss of part of the field of vision

Rare side effects – effects that occur in 1-10 in 10,000 users

- Glaucoma (blockage of fluid in the eye causing increased pressure in the eye, pain or decreased vision)
- Difficulty thinking, remembering information or solving problems, lack of alertness/vigilance, feeling very sleepy and lacking energy – these symptoms may be a sign of a high level of ammonia in the blood (hyperammonemia), which can lead to a change in brain function (hyperammonemic encephalopathy)
- Serious skin reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis – these reactions may appear as a rash with or without blisters, skin irritation, sores and swelling in the mouth, throat, nose, eyes and around the genitals. The skin rash may develop into serious widespread skin damage (peeling of the epidermis and superficial mucous membranes) with life-threatening consequences.

Additional side effects, whose frequency is unknown (effects whose frequency has not yet been determined):

Inflammation of the eye (uveitis) accompanied by symptoms such as eye redness, pain, sensitivity to light, watery eyes, seeing small dots or blurred vision.

Additional side effects, of which the doctor should be informed if they worsen:

Very common side effects – effects that occur in more than 1 user in 10

- Stuffy, runny nose, sore throat
- Tingling, pain and/or numbness of various body parts
- Tiredness or sleepiness
- Dizziness
- Diarrhea
- Nausea
- Weight loss

Common side effects – effects that occur in 1-10 in 100 users

- Anemia (low blood count)
- Allergic reaction (such as skin rash, redness, itching, facial swelling, hives)
- Decreased appetite or loss of appetite
- Aggression, anxiety, anger, abnormal behavior
- Difficulty falling or staying asleep
- Problems with speech, speech disorder, slurred speech
- Clumsiness or lack of coordination, feeling of unsteadiness when walking
- Decreased ability to complete routine tasks
- Decreased/loss of/absence of sense of taste
- Involuntary trembling
- Rapid, uncontrollable movements of the eyes

- Visual disturbances such as double vision, blurred vision, decreased vision, difficulty focusing
- Sensation of spinning (vertigo), ringing in the ears, ear pain
- Shortness of breath
- Cough
- Nosebleed
- Fever
- Weakness
- General unwell feeling
- Vomiting
- Constipation
- Abdominal pain or discomfort
- Indigestion
- Stomach or intestinal infection
- Dry mouth
- Hair loss
- Itching
- Joint pain or swelling
- Muscle cramps or muscle spasms, muscle aches or weakness
- Chest pain
- Weight gain

Uncommon side effects – effects that occur in 1-10 in 1,000 users

- Abnormal blood count, including a decrease in the amount of white blood cells (that help protect against infection) or platelets (blood cells that help stop bleeding) or an increase in the amount of eosinophils (a type of white blood cell)
- Low potassium levels in the blood
- Increased level of liver enzymes
- Swollen glands in the neck, armpit, or groin
- Increased appetite
- Elevated mood
- Hearing, seeing, or feeling things that do not exist, severe mental disorders (psychosis)
- Feeling or displaying apathy, unusual suspiciousness, panic attacks
- Problems with reading, speech disorders, writing problems
- Restlessness or hyperactivity
- Slowed thinking, decreased wakefulness or alertness
- Slow body movements or reduced mobility
- Involuntary abnormal or repetitive muscle movements
- Fainting
- Impaired or abnormal sense of touch
- Impaired, distorted, or no sense of smell
- Unusual feeling or sensation that may precede a migraine or a certain type

of seizure

- Eye problems including dry eyes, sensitivity of the eyes to light, involuntary eyelid twitching, watery eyes
- Decreased or loss of hearing, loss of hearing in one ear
- Unusual or slow heartbeat, palpitations
- Low blood pressure or drop in blood pressure upon standing (consequently, some people taking Topamax may feel faint, dizzy, or may pass out when they stand up or sit up suddenly)
- Hot flushes, feeling warm
- Pancreatitis
- Flatulence, heartburn, feeling of bloating or fullness
- Bleeding gums, increased production of saliva, drooling, bad breath
- Thirst and drinking large amounts of fluids
- Skin discoloration
- Muscle stiffness, side pain
- Blood in urine, urinary incontinence, a sense of urgency in urination, pain in the kidney area
- Sexual dysfunction, difficulty getting or keeping an erection
- Flu-like illness
- Cold sensation in the fingers and toes
- Feeling drunk
- Learning difficulties

Rare side effects – effects that occur in 1-10 in 10,000 users

- Abnormally elevated mood
- Loss of consciousness
- Blindness in one eye, temporary blindness, night blindness
- Lazy eye
- Swelling in and around the eye
- Numbness, tingling and color change (white, blue and red) in fingers and toes when exposed to the cold
- Inflammation of the liver, liver failure
- Bad skin odor
- Discomfort in the arms or legs
- Kidney problems

Additional side effects, whose frequency is unknown (effects whose frequency has not been determined)

- Maculopathy – a disease of the macula area of the eye. This is the small spot in the retina where vision is keenest. If you notice a change or decrease in vision – refer to the doctor.

Side effects in children

The side effects in children are generally similar to those in adults. However, the following side effects may be more common in children than in adults:

- Concentration difficulties
- Increased acid level in the blood
- Thoughts of serious self-harm
- Tiredness
- Decreased or increased appetite
- Aggression, abnormal behavior
- Difficulty falling or staying asleep
- Feeling of unsteadiness when walking
- Unwell feeling
- Decrease in potassium levels in the blood
- Showing or feeling no emotion
- Watery eyes
- Slow or unusual heartbeat

Other side effects that may occur in children:

Common side effects – effects that occur in 1-10 in 100 users

- Sensation of spinning (vertigo)
- Vomiting
- Fever

Uncommon side effects – effects that occur in 1-10 in 1,000 users

- Increased eosinophil (a type of white blood cell) level in the blood
- Hyperactivity
- A feeling of warmth
- Learning difficulties

If a side effect occurs, if one of the side effects worsens, or if you suffer from side effects not mentioned in the leaflet, consult with the doctor.

Side effects may be reported to the Ministry of Health by clicking the link “Report side effects of drug treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il/>

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. Date) that appears on the package. The expiry date refers to the last day of that month.

Storage:

Store below 25°C. Store in the original package and make sure the bottle is tightly closed to protect the tablets from moisture.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Lactose Monohydrate; Microcrystalline Cellulose; Sodium Starch Glycolate; Pregelatinised Starch; Magnesium Stearate; Carnauba Wax

Each Topamax 25 tablet also contains: Opadry White (YS-1-7706-G)

Each Topamax 50 tablet also contains: Opadry Light Yellow (YS-1-6382-G)

Each Topamax 100 tablet also contains: Opadry Yellow (YS-1-6370-G)

Each Topamax 200 tablet also contains: Opadry Pink (YS-1-1456-G)

The lactose monohydrate content in the Topamax 25, 50, 100, 200 mg tablets is:

30.85, 61.70, 123.40, 43.50 mg, respectively.

What does the medicine look like and what are the contents of the package?

Topamax 25 film-coated tablets: a film-coated, round, white tablet, with "TOP" written on one side and "25" on the other side.

Topamax 50 film-coated tablets: a film-coated, round, light yellow tablet, with "TOP" written on one side and "50" on the other side.

Topamax 100 film-coated tablets: a film-coated, round, yellow tablet, with "TOP" written on one side and "100" on the other side.

Topamax 200 film-coated tablets: a film-coated, round, salmon-colored tablet, with "TOP" written on one side and "200" on the other side.

The tablets come in a plastic bottle. Each bottle contains 60 tablets. In each bottle, there is a desiccant – which should not be swallowed.

Registration Holder: J-C Health Care Ltd., Kibbutz Shefayim, 6099000, Israel.

Manufacturer: Cilag AG, Hochstrasse 201 CH-8200, Schaffhausen, Switzerland.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:

Topamax 25 – 107-55-29031

Topamax 50 – 107-56-29032

Topamax 100 – 107-57-29033

Topamax 200 – 107-58-29034

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