PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Levetrim 250
Levetrim 500
Levetrim 1000

Coated tablets

The active ingredient and its quantity:
Each tablet of Levetrim 250 contains levetiracetam 250 mg
Each tablet of Levetrim 500 contains levetiracetam 500 mg
Each tablet of Levetrim 1000 contains levetiracetam 1000 mg

Inactive ingredients and allergens: see section 6 "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any other questions, contact the doctor or the pharmacist.
This medicine has been prescribed to treat your illness. 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 use in babies and children under 4 years of age.

1. What is the medicine intended for?

1. As monotherapy in different types of epilepsy in adults from 16 years of age.
2. As adjunctive therapy to other anti-epileptic medicines in:
   - Adult and pediatric patients from 4 years of age with different types of epilepsy.
   - Adult and adolescent patients from 12 years of age with Juvenile Myoclonic Epilepsy or Idiopathic Generalised Epilepsy.

Therapeutic group: anticonvulsants.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive (allergic) to levetiracetam or other pyrrolidone derivatives or to any of the additional ingredients contained in the medicine (see section 6).

Special warnings regarding the use of the medicine
Before treatment with Levetrim, inform the doctor if:
- You suffer from renal function impairment. The doctor may change the medicine's dosage.
- You observed slower growth or unexpected puberty of your child, contact the attending doctor.
- You experience symptoms of depression and/or suicidal thoughts. A small number of people who were treated with anti-epileptic medicines such as Levetrim have experienced suicidal or destructive thoughts towards themselves.
  Taking anticonvulsants may increase the risk of suicidal actions or thoughts.
  You and your family members must pay attention to changes in mood and behavior patterns. Watch for signs indicating risk of suicide, such as talking or thinking about wanting to hurt yourself, introversion and withdrawal from family and friends, depression or worsening of existing depression, preoccupation with the subject of death, abandoning or giving away prized possessions.
- You or anyone in your family has a history of irregular heart rate (according to an EKG test) or if you have a medical condition or you are taking medicines that can cause irregular heart rate or disturbances in salt balance.
- One of the following side effects worsens or persists for more than a few days:
  - Unusual thoughts, irritability or more aggressive reactions than usual, or if you or your family and people around you observe significant changes in your mood or behavior.
  - Epilepsy worsening: rarely, you may experience increased frequency or worsening of the attacks, particularly during the first month following the beginning of treatment or upon dosage increase. If during treatment the frequency of the attacks increases (e.g., more attacks) or if they worsen, contact the treating doctor as soon as possible. In a very rare form of early-onset epilepsy (epilepsy associated with SCN8A mutations) that causes multiple types of seizures and impairs skills, the seizures may continue or become worse during treatment.

In case one or more of these signs or any other alarming behavioral pattern appears – contact the doctor immediately!

Children and adolescents
Levetrim is not intended to be used as monotherapy for children and adolescents under the age of 16.

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medicines and food supplements, tell the doctor or the pharmacist. Especially if you are taking:
- Macrogol (laxative). Do not take macrogol for an hour before or after taking Levetrim, since it may reduce the medicine's efficacy.
- Temozolomide. Liver function should be evaluated before starting a combination therapy with temozolomide and Levetrim. In case a combination therapy has been decreed, liver function tests should be performed regularly during therapy, and termination of the combined therapy should be considered as necessary.

Use of the medicine and food
The tablets should be taken with a sufficient amount of water (a glass of water).
The medicine may be taken with or without food.

Use of the medicine and alcohol consumption
No data is available regarding interaction between alcohol and this medicine.

Pregnancy and breastfeeding
If you are pregnant, breastfeeding, think you might be pregnant or planning to become pregnant, you should consult the doctor before taking this medicine.
Levetrim may be used during pregnancy, if after careful evaluation the doctor deems this treatment necessary. Do not stop the treatment without consulting a doctor. The risk of causing congenital malformations in the fetus cannot be completely ruled out.
Breastfeeding is not recommended during treatment with Levetrim.

Driving and using machinery
Levetrim may impair your ability to drive or operate dangerous machines, because you might feel drowsy. This effect occurs primarily in the beginning of treatment and after increasing the dose. Do not drive or operate dangerous machines until you feel fit to perform these actions.
Children should be cautioned against riding a bicycle or playing near a road, etc.

3. How should you use the medicine?

Always use the preparation according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation.
The dosage and treatment regimen will be determined by the doctor only.

Do not exceed the recommended dose.

Method of administration
The tablets should be taken with a sufficient amount of water (a glass of water).
The daily dose should be divided into 2 identical doses; one dose should be taken in the morning and one in the evening. Be sure to take the medicine at the same time every day.
Levetrim Tablets is not appropriate for use in children under 6 years of age, due to swallowing difficulties. Levetrim oral solution (100 mg/mL) is the preferred form of administration for children under 6 years old, for children and adolescents (6-17 years old) who weigh less than 50 kg, and when it is difficult to administer an accurate dose with tablets.

Crushing/halving/chewing
Do not chew. The tablet is intended to be swallowed. The tablet may be halved. No information is available regarding crushing/pulverizing the tablet. A crushed tablet may leave a bitter taste.

Duration of treatment
- Levetrim is used as a chronic treatment. Treatment with Levetrim should be continued as long as your doctor instructs you to continue with it.
- Do not discontinue the treatment without an instruction from the doctor, since discontinuing the treatment in this way may increase your seizures.

If you took an overdose or if a child swallowed this medicine by mistake, go to the doctor or the emergency room of the hospital and take the package of the medicine with you. The possible side effects in case of an overdose are drowsiness, irritability, aggressiveness, impaired alertness, respiratory depression and death.

If you have forgotten to take this medicine at the required time, do not take a double dose. Contact the doctor for directions.
Adhere to the treatment as recommended by the doctor.

If you stop taking the medicine:
When discontinuing the treatment, Levetrim should be stopped gradually in order to prevent an increase in seizures.
If the doctor decides to stop the treatment with Levetrim, they will instruct you how to reduce the use gradually.

Do not take medicines in the dark! Check the label and the dose every time you take a medicine. Wear glasses if you need them. If you have any other questions regarding the use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using Levetrim may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Contact the doctor or the nearest emergency room immediately if you experience:
- Weakness, dizziness or difficulty breathing. These may be signs of a severe allergic (anaphylactic) reaction.
- Swelling of the face, lips, tongue and throat (Quincke's edema).
- Flu-like symptoms and facial rash accompanied by disseminated rash with high fever, high levels of liver enzymes and one type of white blood cells (eosinophils) in blood tests, and enlarged lymph nodes (DRESS syndrome).
- Decrease in urine volume, fatigue, nausea, vomiting, confusion and swelling of the legs, ankles and feet. These may be signs of a sudden decrease in renal function.
- A skin rash which may form blisters and look like small targets (dark spots surrounded by a lighter area, surrounded by a darker-shade ring) (erythema multiforme).
- A disseminated rash with blisters and skin peeling, especially around the mouth, nose, eyes and genitalia (Stevens-Johnson syndrome).
- A more severe rash which causes skin peeling in more than 30% of the body surface area (toxic epidermal necrolysis).
- Signs of severe mental changes or if anyone around you observes signs of confusion, sleepiness, memory loss (amnesia), memory impairment (forgetfulness), abnormal behavior or other neurological signs which include involuntary or uncontrolled movements. These may be symptoms of encephalopathy.

The most common side effects are nasopharyngitis, drowsiness, tiredness and dizziness.
Side effects such as sleepiness, fatigue and dizziness may appear more frequently in the beginning of the treatment or when the dosage is increased. These effects usually subside with time.

Very common side effects - side effects that occur in more than one out of ten users:
- Nasopharyngitis.
- Drowsiness, headache.

Common side effects - side effects that occur in 1-10 out of 100 users:
- Lack of appetite (anorexia).
- Depression, hostility or aggressiveness, anxiety, insomnia, irritability or restlessness.
- Spasms, balance disturbances, dizziness, lethargy (a state of lack of energy and lack of enthusiasm), tremor.
- Vertigo (sensation of giddiness).
- Cough.
- Abdominal pain, diarrhea, indigestion, vomiting, nausea.
- Rash.
- Weakness and tiredness.

Uncommon side effects - side effects that occur in 1-10 out of 1,000 users:
- Decreased number of blood platelets, decreased number of white blood cells.
- Decrease or increase in weight.
- Suicide attempt and suicidal thoughts, mental disorder, abnormal behavior, hallucinations, anger, confusion, panic attack, mental imbalance or mood swings, agitation.
- Memory loss (amnesia), memory impairment (forgetfulness) impaired coordination/lack of muscle control (ataxia), numbness (paresthesia), lack of concentration.
- Double vision, blurred vision.
- Abnormal results/increase in liver function test.
- Hair loss, eczema, skin itching.
- Muscle pains, muscle weakness.
- Proneness to injuries.

Rare side effects - side effects that occur in 1-10 out of 10,000 users:
- Infection.
- Decreased number of all types of blood cells.
- Severe allergic reactions (DRESS, anaphylactic reaction [a severe allergic reaction], Quincke's edema [swelling of the face, lips, tongue and throat]).
- A decrease in blood sodium concentration.
- Suicide, personality disorders, thinking disturbances (slow thinking, inability to concentrate).
- Delirium.
- Encephalopathy (see section "Contact the doctor or the nearest emergency room immediately if you experience" for detailed description of the symptoms).
- Worsening of the attacks or increased frequency.
- Uncontrollable muscle spasms, which affect the head, torso and limbs, difficulty in controlling movement, excessive movements (hyperkinesia).
- Altered heart rate (EKG).
- Inflammation of the pancreas (pancreatitis).
- Liver failure, inflammation of the liver (hepatitis).
- Sudden decrease in renal function.
- Skin rash (erythema multiforme) which may be manifested as small target-like blisters (dark dots in the middle, surrounded by a lighter area, surrounded by a darker-shade ring), disseminated rash with blisters and skin peeling, especially around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome), or a more severe form that causes peeling of more than 30% of the skin surface area (toxic epidermal necrolysis).
- Rhabdomyolysis (muscle tissue breakdown) and rise in creatine phosphokinase blood levels. This effect is more common in Japanese than non-Japanese patients.
- Limping or difficulty walking.
- Combination of fever, muscle rigidity, unstable blood pressure and heart rate, confusion, decrease in the level of consciousness (possible signs of a disturbance known as neuroleptic malignant syndrome). It is more likely to develop in Japanese patients than in non-Japanese patients.

Very rare side effects - side effects that occur in up to 1 in 10,000 users:
- repeated uncontrolled thoughts or sensations or the urge to do something over and over again (Obsessive Compulsive Disorder).

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.
Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il
You can also report to the email: safety@trima.co.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Store in a dry place at a temperature below 25°C. Store in the original package.

6. Additional information:

In addition to the active ingredient, the medicine also contains:
Maize starch, povidone, hypromellose, titanium dioxide, colloidal silicone dioxide, magnesium stearate, polyethylene glycol.

What does the medicine look like and what are the contents of the package:
Levetrim 250: a white, round, biconvex film-coated tablet with a score line on one side.
Levetrim 500: a white, oblong, biconvex film-coated tablet with a score line on one side.
Levetrim 1000: a white, oval, biconvex film-coated tablet with a score line on one side.
The tablets are packed in aluminum blisters. Each package contains 60 tablets.
Manufacturer's and License Holder's name and address: Trima Israel Pharmaceutical Products Maabarot Ltd., Maabarot 4023000, Israel
Revised in August 2023 in accordance with the Ministry of Health guidelines.
Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
Levetrim 250: 143.75.31935.00
Levetrim 500: 143.76.31936.00
Levetrim 1000: 143.77.31941.00

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