

Frisium

Tablets, 10 mg

Active ingredient:

Each tablet contains:

Clobazam 10 mg

Inactive ingredients: See section 2 – 'Important information about some of the ingredients of the medicine' and section 6 – 'Further Information'.

Read this leaflet carefully in its entirety before using this 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.

Introduction to the patient leaflet for benzodiazepines

- This medicine belongs to the benzodiazepine group, which has special characteristics which require a lot of caution during use.
- It is very important to be under close medical supervision when taking this medicine.
- When you are taking this medicine, be sure to refer to a doctor after 2-4 weeks, as the treatment is meant for short periods only.
- Prolonged use of the medicine may reduce the effect of the medicine.
- Such use may cause a severe dependence effect, which will make it hard for the patient to stop taking the medicine.
- Unregulated discontinuation of treatment is accompanied with withdrawal effects, such as: tension, irritability, confusion, tremor, insomnia, abdominal pains, vomiting, nausea, sweating, spasms.
- Sometimes, prolonged use of the medicine may cause behavioral changes and bothersome thoughts.
- It is recommended, especially for the elderly, to be careful when walking, as the medicine impairs alertness and sometimes body movement coordination, and there is therefore danger of tripping or falling.

Taking this medicine with opioids, other medicines that suppress the central nervous system (including drugs) or alcohol, may cause deep sleepiness, breathing difficulties (respiratory depression), coma and death.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is used for treatment of states of anxiety in adults.

Therapeutic group: The active ingredient belongs to a group of medicines called benzodiazepines.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient, to other benzodiazepines or to any of the additional ingredients contained in the medicine (see section 6).
- Signs of an allergic reaction include: rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- You are pregnant or are planning a pregnancy (see below under 'Pregnancy, breastfeeding and fertility' for further information)
- You are breastfeeding
- You have ever had problems with drugs or alcohol dependence
- You have a disease which causes muscle weakness (called myasthenia gravis)
- You have liver problems
- You have breathing problems
- You stop breathing for short periods during sleep (called 'sleep apnea syndrome')

Do not take the medicine if one of the above conditions applies to you. If you are uncertain, speak to your doctor or pharmacist before taking Frisium.

Special warnings regarding use of the medicine

Before treatment with Frisium, tell the doctor if:

- You have a problem controlling your movements (called 'spinal or cerebellar ataxia').
- You suffer from depression, irrational fears and compulsive thoughts.
- You have delusions (believing things which are not true) or hallucinations (sensing things which are not there).
- You have kidney problems.
- You developed a dependence on another medicine or on alcohol in the past. Do not consume alcohol during the course of treatment with Frisium due to increased risk of side effects.
- You are above the age of 65 years. This is because of an increased risk of side effects in the elderly, such as drowsiness, dizziness and muscle weakness. There is also an increased risk of falls, which may cause serious injury.
- You have difficulty digesting medicines. In some patients, the liver may not metabolize (break down) medicines adequately. In these patients, the medicine may remain in the body for a longer period of time. This may cause side effects. If you know that your metabolism of certain medicines is impaired, please speak to your doctor.
- You are taking any medicinal or non-medicinal products containing cannabidiol, as it may increase the side effects of clobazam.

The medicine, especially when taken with other medicines, including medicines to treat epilepsy, may cause serious and life-threatening skin side effects. If they occur, refer to the doctor immediately.

Drowsiness, breathing difficulties, coma and death may occur if Frisium is taken together with opioids. Frisium and opioids can only be used

concomitantly when other treatment options are unsuitable. Please tell your doctor about all the opioids you are taking and be sure to closely follow the doctor's instructions regarding dosage.

Certain studies have shown an increased risk of suicidal thoughts, suicide attempts and suicide in patients taking certain sedatives and hypnotics, including this medicine. However, it has not been established whether this is caused by the medicine or if there may be other reasons. If you have suicidal thoughts, contact your doctor as soon as possible for additional medical advice (see section 4 "Side Effects").

If you are not sure if one of the above conditions applies to you, speak with your doctor or pharmacist before taking Frisium.

Children and adolescents

This medicine is not intended for children.

Tests and follow-up

If there is a need to start treatment with a medicine containing the active ingredient stiripentol, in addition to Frisium, blood tests will be necessary before starting and during treatment. Close medical surveillance is necessary in the first eight weeks of treatment to immediately identify onset of severe skin side effects.

Drug interactions

If you are taking, may take or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. This is because Frisium may affect the way certain other medicines work. In addition, certain medicines may affect the way Frisium works.

Especially, inform the doctor if you are taking:

- Medicines for epilepsy (such as phenytoin, carbamazepine, stiripentol or valproic acid).
- Medicines for depression (such as monoamine oxidase inhibitors (MAOIs) or tricyclic antidepressants, such as trazodone, or selective serotonin reuptake inhibitors (SSRIs), such as fluvoxamine or paroxetine).
- Medicines for severe mental illness called 'antipsychotics' (such as chlorpromazine, haloperidol, clozapine and pimozide).
- Painkillers (such as medicines containing codeine, dihydrocodeine or morphine).
- Sleep medicines (such as zolpidem).
- Tranquilizers (such as diazepam, temazepam or lorazepam).
- Muscle relaxants (such as baclofen).
- Antihistamines that cause you to be sleepy (such as chlorphenamine, promethazine or diphenhydramine).
- Lithium – used for a mental illness called 'manic-depression' (mood changes between a state of high excitability or exaggerated emotions and depression).
- Cimetidine – used to treat ulcers and heartburn.
- Omeprazole – used to treat stomach conditions.
- Ticlopidine – a medicine which inhibits platelet aggregation, used to prevent blood clots.
- Fluconazole – used to treat fungal conditions.
- Dextromethorphan – used to relieve dry and irritating cough.
- Nebivolol – used to treat high blood pressure.
- Cannabidiol-containing products (medicinal or non-medicinal products). Concomitant use of Frisium and opioids increases the risk of drowsiness, breathing difficulties, coma and death. Follow the doctor's instructions regarding dosage closely. If you are unsure if one of the above conditions applies to you, talk to your doctor or pharmacist.

Anesthetics

If you are due to receive an anesthetic, tell your doctor or anesthetist that you are taking Frisium. This is because your doctor may need to change the amount of anesthetic or muscle relaxant to give you.

Use of the medicine and alcohol consumption

Do not drink alcohol while taking Frisium. This is because there is an increased risk of sleepiness and other side effects.

Pregnancy, breastfeeding and fertility

Use of this medicine is not recommended during pregnancy and in women of childbearing potential not using contraception.

If you discover that you are pregnant or are planning a pregnancy, consult your doctor immediately to reassess the need for treatment. Do not stop taking Frisium without talking to your doctor.

A large amount of data has not shown evidence of malformations associated with the use of benzodiazepines. However, some studies have shown a potentially increased risk of cleft lip and palate in newborn babies compared to that in the general population.

Cleft lip and palate (sometimes called "harelip") is a birth defect caused by incomplete fusion of the palate and upper lip.

Reduced fetal movement and fetal heart rate variability may occur after taking clobazam during the second and/or third trimester of pregnancy. If Frisium is taken at the end of pregnancy or during childbirth, your baby may show drowsiness, muscle weakness (hypotonia or muscle flaccidity), a drop in body temperature (hypothermia), difficulty feeding (problems suckling causing poor weight gain) and breathing problems (respiratory depression, sometimes severe).

If the medicine is taken regularly in the late stages of pregnancy, your baby may get withdrawal symptoms such as agitation or shaking. In this case, the newborn should be closely monitored during the postnatal period. Do not take Frisium if you are breastfeeding or are planning to breastfeed. This is because it may pass into the breast milk.

Driving and operating machinery

You may feel sleepy or have concentration or memory problems after taking this medicine. You may also suffer from double vision or you may react to things more slowly. If this happens, do not drive or use tools or machines.

The medicine may affect your ability to drive, since it may cause you to be sleepy or dizzy.

Do not drive while using this medicine until you know how it affects you. Talk to your doctor or pharmacist if you are unsure if it is safe for you to drive while taking the medicine.

Important information about some of the ingredients of the medicine
Frisium contains lactose. If you have been told by your doctor that you have an intolerance to certain sugars, talk to your doctor before taking the medicine.

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 preparation dosage and treatment regimen.

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

Do not exceed the recommended dose.

Take this medicine for as long as the doctor prescribes it for you.

If you feel that the effect of the medicine is too strong or too weak, do not change the dosage on your own; consult the doctor.

Frisium is usually given for a period of 2-4 weeks; afterwards, the doctor will decide whether the treatment should be continued.

The recommended dosage for adults: 20-30 mg per day in two divided doses or as a single dose at night.

The doctor may increase the dosage to up to 60 mg per day and the doctor may lower the dosage.

The recommended dosage for the elderly: 10-20 mg per day.

This medicine is not intended for children.

Patients suffering from liver or kidney problems will take a low dosage of Frisium, as per the doctor's instructions.

The doctor will decide on further treatment after no more than 4 weeks from the start of treatment.

Do not chew! Swallow the medicine whole with at least half a glass of water or crushed and mixed in apple sauce.

The tablet can be halved to obtain a dosage of 5 mg.

If the preparation is taken a few times a day, take the higher dose in the evening.

If you accidentally took a higher dosage:

If you took an overdose, or if a child has accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you. Do not drive, as you may feel sleepy.

If you forget to take the medicine:

If you forgot to take this medicine at the required time, take a tablet as soon as you remember, but if it is almost time for the next tablet, skip this dose. **Do not** take a double dose to compensate for the forgotten tablet. Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with this medicine without consulting a doctor.

Discontinuation of treatment will be done gradually.

If you stop taking the medicine:

Discontinuation of treatment with the medicine can cause restlessness, anxiety, confusion, depression and even loss of appetite and difficulty sleeping. Tell the doctor if this happens.

Do not stop taking this medicine unless a doctor has instructed you to do so. Discontinuation of treatment with the medicine will be done gradually. Refer to a doctor before discontinuing treatment.

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 Frisium may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

You may feel ill after taking the tablets, or notice unusual or unexpected symptoms. If this happens, tell your doctor.

Refer to a doctor immediately if one of the following side effects appears:

Common side effects (may affect up to 1 in 10 users):

- Feeling irritable or restless.

Uncommon side effects (may affect up to 1 in 100 users):

- Poor memory while taking Frisium (amnesia) or unusual behavior.
- Nightmares.
- Feeling anxious.
- Believing things which are not true (delusions).
- Increased possibility of tripping or falling, especially in elderly patients.

Side effects of unknown frequency (frequency cannot be estimated from available data):

- Sleeping problems that get worse after taking the medicine.
- Sensing things which are not there (hallucinations).
- Being less aware of your environment, especially in the elderly.
- Feeling suicidal.
- Blistering or bleeding of the skin around the lips, eyes, mouth, nose and genitals. In addition, flu-like symptoms and fever. This may be 'Stevens-Johnson syndrome'.
- A severe blistering rash where layers of the skin may peel off to leave widespread areas of raw exposed skin over the body. Also, a feeling of being generally unwell, fever, chills and aching muscles. This is called 'toxic epidermal necrolysis'.

If you get any of the above side effects, your doctor may decide that your treatment needs to be stopped. These side effects are more common in elderly people.

Refer to your doctor or pharmacist if one of the following side effects worsens or lasts longer than a few days, or if you notice any side effects not listed in the leaflet.

Very common side effects (may affect more than 1 in 10 users):

- Difficulty in staying awake or alert.

Common side effects (may affect up to 1 in 10 users):

- Feeling sleepy or dizzy.
- Feeling agitated or aggressive.
- Depression.
- Headache.
- Short attention span.
- Difficulty in speaking.
- Shaking fingers (tremor).
- Problems with walking or other movement problems.
- Lower effect of Frisium than normal (especially in long-term use).
- Dry mouth, constipation.
- Loss of appetite, nausea.

Uncommon side effects (may affect up to 1 in 100 users):

- Loss of sexual drive.
- Memory difficulties, confusion.
- Double vision.
- Skin rash.
- Weight gain.

Side effects of unknown frequency (frequency cannot be estimated from available data):

- Becoming dependent on Frisium (physical or mental dependence) (especially in long-term use).
- A feeling of being out of touch with reality and inability to think or judge clearly (psychosis).
- Feeling angry.
- Changes in the way you walk.
- Breathing problems.
- Sensitivity to sunlight.
- Itchy, lumpy rash (urticaria).
- Muscle spasms or muscle weakness.
- Reacting to things more slowly than usual.
- Rapid uncontrollable movement of the eyes.
- Learning problems.
- Abnormally low body temperature.
- Urinary retention.

The following side effects are more likely to happen at the start of treatment. They usually last for a short time: feeling tired, dry mouth, constipation, loss of appetite, feeling sick, shaking fingers.

If you take the medicine for a long time, you are more likely to get the following side effects: anxiety, confusion, depression, loss of appetite and difficulty sleeping.

After discontinuing treatment, isolated incidents of a withdrawal-like effect may occur, particularly at high dosages or after prolonged treatment (if authorized by the doctor). If you feel withdrawal effects, such as those detailed in the introduction, or any other effect, consult a doctor.

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

Side effects can be reported to the Ministry of Health by clicking on 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 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. Store at a temperature below 25°C.

Do not discard medicines in the wastewater or household waste. Ask your pharmacist how to dispose of medicines that are no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains: Lactose monohydrate, maize starch, talc, colloidal anhydrous silica, magnesium stearate.

What the medicine looks like and the contents of the package

The tablets are round and white, with a score line and a "B" imprinted on one side of the score line and "GL" on the other side of the score line. A logo is imprinted on the other side of the tablet.

Frisium is packaged in a blister pack of 10, 20 or 30 tablets. Not all pack sizes may be marketed.

License holder and importer and address

sanoofi-aventis Israel Ltd., P.O.B. 8090, Netanya
Revised in August 2021 according to MOH guidelines.
Registration number of the medicine in the National Drug Registry of the Ministry of Health: 125-90-24542