

Patient Package Insert accompanying
Pharmacists' Regulations (Preparations)-1986
This medicine can be sold with a physician's prescription only

Xanagis 0.25 mg
Tablets

Xanagis 0.5 mg
Tablets

Xanagis 1 mg
Tablets

Each tablet contains:
Alprazolam 0.25 mg
Alprazolam 0.5 mg
Alprazolam 1 mg

Inactive ingredients and allergens: See in section 6 "Additional information" and in section 2 "Important information about some of the ingredients of this medicine".

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

This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It might harm them, even if you think that their medical condition is similar.

What is the most important information I need to know about the medicine?

Taking this medicine with medicines from the opioid family, other central nervous system depressants (including drugs) or alcohol may cause a sense of deep drowsiness, breathing difficulty (respiratory depression), coma and death.

Introduction to the benzodiazepines patient leaflet

This medicine belongs to the benzodiazepines group, which has special characteristics necessitating great caution with its use.

- Close medical monitoring is very important when taking this medicine.
- When you take this medicine, be sure to refer to the doctor after 2-4 weeks, as the treatment is meant for short periods only.
- Prolonged use of the medicine may cause the medicine's effect to decrease.
- Prolonged use may cause severe dependence, which will make it difficult for the patient to stop taking the medicine.
- Uncontrolled discontinuation of treatment may be accompanied by withdrawal symptoms, such as: tension, nervousness, confusion, tremor, insomnia, abdominal pain, vomiting, nausea, sweating, spasms, muscle cramps and pain.
- Sometimes, prolonged use of the medicine may cause changes in behavior patterns and obsessive thoughts.
- Especially with the elderly, it is recommended to be careful when walking because the medicine impairs alertness and sometimes motor coordination and therefore there is a risk of tripping or falling.

1. What is the medicine intended for?

Xanagis is intended for treatment of anxiety accompanied by depression. Treatment of states of panic that are or are not accompanied by phobia.

Therapeutic group: Benzodiazepines

2. Before using the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient alprazolam, to other benzodiazepines or to any of the other ingredients this medicine contains. For the list of inactive ingredients, see section 6 "Additional Information".
- You are taking medicines to treat fungal infections including ketoconazole and itraconazole.

Special warnings regarding the use of this medicine

Before taking Xanagis, tell the doctor if:

- you suffer or have suffered from depression, mood changes, suicidal thoughts or suicidal behavior.
- you suffer from liver or kidney problems.
- you suffer from a lung disease or breathing problems.
- you are pregnant or are planning a pregnancy (see below "Pregnancy and breastfeeding").
- You are breastfeeding or planning to breastfeed (see below "Pregnancy and breastfeeding").
- you suffer from or have suffered in the past from abuse of or dependence on alcohol, prescription medicines or drugs.

Children and adolescents

Xanagis is not intended for use in children and adolescents under 18 years of age, as there is no information regarding the safety and effectiveness of the use of this medicine in children and adolescents.

Smoking

Smoking reduces the medicine's concentration in the body in comparison to non-smokers.

Use in the elderly

Elderly patients are especially susceptible to dosage related side effects while using Xanagis.

Pregnancy and breastfeeding

Pregnancy

Consult your doctor if you are pregnant or are planning a pregnancy, as Xanagis may harm your fetus. Your doctor must decide if you should take Xanagis while pregnant.

Breastfeeding

Consult your doctor if you are breastfeeding or planning to breastfeed. Do not breastfeed while taking Xanagis, as Xanagis passes into your breast milk and may harm your baby. Talk to your doctor about the best way to feed your baby if you are taking Xanagis.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines, vitamins and nutritional supplements, tell the doctor or pharmacist.

Especially if you are taking:

- opioids, as concomitant use with Xanagis may increase the risk of respiratory depression (see at the beginning of this leaflet "What is the most important information I need to know about the medicine?").
- antifungal medicines (e.g., ketoconazole and itraconazole) (see at the beginning of this section "Do not use the medicine if;").
- medicines to treat anxiety or depression (e.g., nefazodone, fluvoxamine, fluoxetine, paroxetine, sertraline).
- the narcotic analgesic propoxyphene.
- contraceptive pills.
- medicines to treat epilepsy (e.g., carbamazepine).
- antipsychotic medicines used to treat mental illnesses such as schizophrenia.
- antihistamines used to relieve allergies.
- certain antibiotics of the macrolide family (e.g., erythromycin, clarithromycin).
- isoniazid (to treat tuberculosis).
- cimetidine (to treat stomach ulcers).
- tricyclic antidepressants (e.g., imipramine, desipramine).
- calcium channel blockers (e.g., diltiazem, nicardipine, nifedipine).
- cyclosporine.
- ergotamine (to prevent and treat migraine).
- amiodarone (to treat arrhythmia).
- drugs or additional medicines that cause drowsiness or dizziness. Xanagis may make the drowsiness or dizziness worse, when taken with drugs or medicines that cause drowsiness or dizziness.

Use of this medicine and food

Grapefruit juice may increase the concentration of Xanagis in the blood.

Use of this medicine and alcohol consumption

Do not drink alcohol or take other medicines that may cause you drowsiness or dizziness while taking Xanagis, without consulting your doctor. When Xanagis is taken together with alcohol or medicines that cause drowsiness or dizziness, Xanagis may make your drowsiness or dizziness worse.

Driving and use of machinery

Xanagis may cause you to be sleepy or dizzy and slow your thinking and motor skills. Do not drive, operate dangerous machinery, or engage in dangerous activities, until you know how Xanagis affects you.

Important information about some of the ingredients of this medicine

Xanagis contains lactose monohydrate, which is a type of sugar. If you have been told by your doctor that you have an intolerance to certain sugars, contact your doctor before taking this medicine.

This medicine contains 0.11 mg sodium benzoate in each tablet. Sodium benzoate may make jaundice (yellowing of the skin and eyes) worse in newborns (up to 4 weeks old).

This medicine contains less than 23 mg sodium per tablet, that is to say essentially sodium-free.

3. How to use this medicine

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and manner of treatment with the product.

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

The usual recommended dosage is:

In adults:

Anxiety: Usually treatment will begin with taking one 0.25 mg tablet or one 0.5 mg tablet 3 times daily. Accordingly, the daily dosage will include 0.75 mg to 1.5 mg. This dosage can increase gradually (every 3-4 days the dose can be increased by 1 mg) until a daily total dosage of 3 mg, divided throughout the day. The dosage can be increased to achieve the maximum therapeutic effect, at intervals of 3 to 4 days, to a maximum daily dosage of 4 mg, which will be given in divided doses.
Panic: Usually treatment will begin with taking one tablet of 0.5 mg 3 times daily. This dosage can increase gradually depending on the reaction (every 3-4 days the dose can be increased by 1 mg) until a daily dose greater than 4 mg, divided throughout the day.

When it is necessary to increase the dose, it is customary to first increase the nighttime dose, before increasing the daytime dose, to ensure that you are more alert during the day. If you start to experience side effects, the doctor may reduce the dosage.

Elderly or patients suffering from a debilitating disease: The usual starting dose is 0.25 mg two to three times daily. This dosage can be increased gradually, according to the doctor's instructions, if necessary, and if you do not suffer from side effects.

Do not exceed the recommended dose.

Duration of treatment

Xanagis is intended for short term treatment (no more than 8-12 weeks). The doctor will usually evaluate your condition at the very latest at the end of 4 weeks and decide if it necessary to continue treatment.

In certain cases, in accordance with a specialist's assessment, it may be necessary to extend the treatment beyond the maximum treatment period. Reduced effect of the treatment may develop if it is used for more than several weeks.

Method of administration

There is no information about crushing/halving/chewing. To ease swallowing, the tablet can be halved for immediate use, if necessary. Swallow the two halves together immediately after halving.

If you have accidentally taken a higher dosage, you may suffer from drowsiness, confusion, impaired coordination, reduced reflexes and coma. Death has also been reported. If you have taken an overdose or if a child or anyone else has accidentally swallowed the medicine, proceed immediately to the doctor or to a hospital emergency room and bring the package of the medicine with you.

If you forget to take this medicine at the set time, take it as soon as you remember, unless it is almost time to take the next dose. Never take a double dose to compensate for a forgotten one.

Do not increase the dosage without consulting the doctor, even if you think that you are not responding to the medicine. Medicines of the benzodiazepine group may cause emotional or physical dependence, even if they were recommended for your use.

If you stop taking this medicine

• Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor, as the dosage must be decreased gradually.

• **Physical dependence and withdrawal reactions.** Xanagis can cause physical dependence and withdrawal reactions.

- If you stop taking the tablets abruptly (and not gradually), you may have serious and life- threatening side effects, including abnormal movements, responses or expressions, seizures, severe mental or nervous system changes, depression, seeing or hearing things that others do not see or hear, an extreme increase in activity or talking, losing touch with reality and suicidal thoughts or actions. **Contact your doctor or proceed to the nearest hospital emergency room immediately, if you have any of these symptoms.**

- Some patients who suddenly (not gradually) stop taking benzodiazepines may have side effects that can last for several weeks to more than 12 months, including anxiety, trouble remembering, learning or concentrating, depression, problems sleeping, feeling like insects are crawling under the skin, weakness, shaking, muscle twitching, burning or prickling feeling in the hands, arms, legs and feet, and ringing in the ears.
- In addition, you may have withdrawal symptoms (see section 4 "Side effects").

Continue with the treatment as recommended by the doctor.

Do not take medicines in the dark! Check the label and the dose **each time** you take a 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, the use of Xanagis may cause side effects in some users. Do not be alarmed while reading the list of side effects. You might not suffer from any of them.

Side effects with Xanagis, if they occur, are usually seen at the beginning of the treatment and usually disappear with continued medication.

Xanagis may cause serious side effects, which include:

(see at the beginning of this leaflet "What is the most important information I need to know about the medicine?").

- **Risk of abuse, misuse, and addiction.** There is a risk of abuse, misuse, and addiction with benzodiazepines, including Xanagis, which can lead to overdose and serious side effects including coma and death.

- **Serious side effects including coma and death have happened in people who have abused or misused benzodiazepines including Xanagis.** These serious side effects may also include delirium, paranoia, suicidal thoughts or actions, seizures, and difficulty breathing. **Contact your doctor or proceed to the nearest hospital emergency room immediately, if you suffer from any of these serious side effects.**

- **You can develop an addiction even if you take Xanagis according to the instructions of your doctor.**

- **Seizures.** Discontinuing Xanagis can cause seizures and seizures that will not stop (status epilepticus).

- **Mania.** Xanagis can cause increased activity and speech (hypomania and mania) in people suffering from depression.

Seek emergency medical assistance immediately in the following cases:

- Slowed breathing or shallow breathing
- Respiratory arrest (may lead to cardiac arrest)
- Excessive drowsiness

The most common side effects of Xanagis include drowsiness and lightheadedness.

Additional Side Effects:

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

Drowsiness, lightheadedness, depression, headache, dry mouth, constipation, diarrhea, fatigue and tiredness, coordination problems, nervousness, memory impairment, dizziness, insomnia, cognitive disorder, speech disorder (dysarthria), anxiety, abnormal involuntary movements, decreased libido, confusion, decreased salivation, nausea, vomiting, abdominal discomfort, nasal congestion, rapid heart rate (tachycardia), chest pain, blurred vision, sweating, rash, increased appetite, decreased appetite, weight gain, weight loss, difficulty urinating, menstrual irregularities.

Common side effects (may affect up to 1 user out of 10): Confusion, insomnia, irritability, fainting, dizziness, physical restlessness (akathisia), nausea, vomiting, increased salivation, rapid heart rate (tachycardia), palpitations, low blood pressure, blurred vision, stiffness, tremor, dermatitis, allergy, nasal congestion, weight gain, weight loss, muscle spasm, increase in libido, change in libido (non-specific), weakness, muscle tone disorders, restlessness (agitation), disinhibition, paresthesia, talkativeness, vasomotor disorders, derealization, abnormal dreams, fear, feeling warm, hyperventilation, upper respiratory tract infection, tinnitus (noises in the ears), muscle cramps, muscle stiffness, sexual dysfunction, edema, urinary incontinence, infection.

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

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report adverse effects and problems associated with medications" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or by clicking on the following link:

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

Additionally, side effects can be reported to Perrigo via the following address: www.perrigo-pharma.co.il

5. How to Store the Medicine

- **Avoid poisoning!** This medicine, and all other medicines, must be stored 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) that appears on the carton package and the blister it contains. The expiry date refers to the last day of that month.
- Store in a cold place below 25°C. Protect from light.

6. Additional Information

- In addition to the active ingredient, the medicine also contains the following inactive ingredients:

Xanagis 0.25 mg:

Lactose monohydrate, Microcrystalline cellulose, Maize starch, Docusate sodium (85%) + Sodium benzoate (15%), Magnesium stearate, Colloidal anhydrous silica.

Xanagis 0.5 mg:

Lactose monohydrate, Microcrystalline cellulose, Maize starch, Docusate sodium (85%) + Sodium benzoate (15%), Magnesium stearate, Colloidal anhydrous silica, Erythrosine sodium aluminum lake.

Xanagis 1 mg:

Lactose monohydrate, Microcrystalline cellulose, Maize starch, Docusate sodium (85%) + Sodium benzoate (15%), Magnesium stearate, Colloidal anhydrous silica, Erythrosine sodium aluminum lake, F.D. and C. Blue Nr.2 aluminum lake.

- **What the medicine looks like and contents of the package:** The medicine is supplied in carton packages containing 10/30/50 tablets in blisters (trays). Each blister contains 10 tablets.

Xanagis 0.25 mg: Oval, white tablets with a score line on one side and "UPJOHN 29" imprinted on the other side.

Xanagis 0.5 mg: Oval, pink tablets with a score line on one side and "UPJOHN 55" imprinted on the other side.

Xanagis 1 mg: Oval, light purple tablets with a score line on one side and "UPJOHN 90" imprinted on the other side.

Manufacturer, registration holder and address: Perrigo Israel Pharmaceuticals Ltd., P.O.B. 16, Yeruham.

- Revised in April 2021 according to MOH guidelines.

Drug registration number at the national medicines registry of the Ministry of Health:

Xanagis 0.25 mg: 063 48 26906

Xanagis 0.5 mg: 063 46 26908

Xanagis 1 mg: 063 47 26907

Xanagis 0.25 0.5 1 mg PIL PB0621-06