PACKAGE LEAFLET

Package leaflet: Information for the user

Alprazolam Krka 0.5 mg prolonged-release tablets
Alprazolam Krka 1 mg prolonged-release tablets
Alprazolam Krka 2 mg prolonged-release tablets
alprazolam

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Alprazolam Krka is and what it is used for

The active ingredient is alprazolam. It belongs to the group of medicines called benzodiazepines (anxiety-relieving medicines).

Alprazolam Krka tablets are used in adults for treatment of anxiety symptoms which are severe, disabling or causing the patient great distress. This medicine is for short-term use only.

2. What you need to know before you take Alprazolam Krka

Do not take Alprazolam Krka if you
- are allergic to alprazolam, other benzodiazepines or any of the other ingredients of this medicine (listed in section 6)
- have been diagnosed with *myasthenia gravis* (a disease causing muscle weakness)
- suffer from severe respiratory failure
- have sleep apnoea syndrome (prolonged transient cessations of breathing during sleep)
- suffer from severe liver insufficiency.

Warnings and precautions

Talk to your doctor before taking Alprazolam Krka tablets, if you
- notice that the effect of the tablets will weaken after you have used them several weeks (tolerance)
- are worried of the physical and mental dependence caused by aprazolam. If you do not want to suspend the treatment, you may be mentally dependent to this medicine. If there is physical dependence, the suspension of treatment is accompanied by withdrawal symptoms (see section 3, If you stop taking Alprazolam Krka tablets). The risk of dependence is greater as the dose and the length of treatment increase in patients with history of alcohol or drug abuse or if several benzodiazepines are combined. To reduce the risks, the dose should be as low as possible and

the duration of treatment as short as possible. Follow your doctor's dose recommendations.
- a history of alcohol, drug or narcotic abuse
- have had memory disorders. Loss of memory usually occurs several hours after the product has been taken.
- get unexpected reactions e.g. restlessness, agitation, irritability, aggresivness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour, delirium and other behaviour disorders. These unexpected reactions occur more often in children and elderly patients.
- a chronic lung disease
- if you are using concomitantly alcohol and sedative drugs
- been diagnosed with renal or liver function impairment
- been diagnosed with some psychiatric illness
- are elderly. Benzodiazepines should be used with caution in elderly, due to the risk of sedation and / or muscle weakness that can promote falls.

Abuse
Drug abuse is a known risk with this drug (see also section 4 "Possible side effects"). Abusing this drug can lead to overdose and death. Always follow your doctor's dose recommendations. This medicine may be desirable for people who abuse prescription drugs, and should be kept out of reach of other people.

Effect on mood
The treatment with Alprazolam Krka may increase the risk of hypomania or mania in patients with depression. Please contact your doctor immediately if you notice symptoms of mania or hypomania.

The treatment with Alprazolam Krka may increase the risk to develop thoughts of harming or killing yourself if you suffer from:
- depression.

Please ask your doctor before starting treatment with Alprazolam Krka.

If treatment with Alprazolam Krka is necessary and if you are depressed or have previously had thoughts about killing or harming yourself your doctor will monitor you closely. If you develop thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.

<u>If you are going to have an operation</u>
Tell your doctor that you are taking Alprazolam Krka.

Children and adolescents
The safety and efficacy of alprazolam in patients under 18 years old has not been established. Therefore, use of alprazolam is not recommended in this age group.

Other medicines and Alprazolam Krka
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Some medicines may cause undesirable effects if taken at the same time as alprazolam. If you are simultaneously taking certain other medicines, this may affect the efficacy of the treatment. In this case, your doctor may adjust your medication or the dosage instructions.
Such medicines include:

Medicines, which increase the sedative effect of alprazolam:
- sleeping pills and sedatives
- antipsychotics and antidepressants
- antiepileptics
- strong painkillers that act through the central nervous system
- sedative antihistamines

Medicines, which increase the effect of alprazolam, because they reduce its metabolism in the liver:
- nefazodone, fluvoxamine , fluoxetine, sertralin (medicines for severe depression)
- cimetidine (used for treating stomach problems)
- medicines used for treating HIV
- dextropropoxyphene
- oral contraceptives
- diltiazem (blood pressure and heart medicine)
- certain antibiotics (e.g., erythromycin, clarithromycin, telithromycin and troleandomycin) and certain medicines for treating fungal infections (e.g., itraconazole, ketoconazole, posaconazole, voriconazole)

Medicines, which decrease the effect of alprazolam, because they increase its metabolism in the liver:
- carbamazepine or phenytoine (antiepileptics, which are used also for other treatments)
- St John's wort (*Hypericum perforatum,* a herbal remedy)
- rifampicin (antituberculosis drug)

Alprazolam can increase the effect of the following medicines:
- digoxin (heart medicine)
- muscle relaxants
- imipramine and desipramine (medicines for severe depression)
- clozapine (psychosis medicine). There is an increased risk of respiratory and/or cardiac arrest.

Alcohol potentiates the sedative effect of alprazolam.

Concomitant use of Alprazolam Krka and opioids (strong pain killers, medicines for substitution therapy and some cough medicines) increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible.
However if your doctor does prescribe Alprazolam Krka together with opioids the dose and duration of concomitant treatment should be limited by your doctor.
Please tell your doctor about all opioid medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

The next time you visit your doctor, please remember to tell him or her you are taking Alprazolam Krka tablets.

Alprazolam Krka with food, drink and alcohol
Take the tablet with a glass of water or some other fluid.

Alcohol
Do not drink any alcohol while you are taking Alprazolam Krka tablets.

Pregnancy and breast-feeding
If you are pregnant or planning to get pregnant, or if you are breast-feeding, ask your doctor for advice before taking Alprazolam Krka.

Alprazolam Krka should not be used during pregnancy unless the doctor considers it absolutely necessary for the mother's treatment.
There are no adequate experiences from the use of alprazolam in pregnant women. Do not take Alprazolam Krka if you are pregnant or planning to become pregnant, unless your doctor considers it strictly indicated. Observations in humans have indicated that the substance alprazolam can be harmful to the unborn child(increased risk of malformations (oral clefts). If you are pregnant or planning a pregnancy, consult your doctor about the possibility to stop the treatment.If you are taking Alprazolam Krka until birth, let your doctor know as your newborn might have some withdrawal symptoms when

it is born. A high-dose use in late pregnancy or during labor may cause the newborn also lowered body temperature, cause respiratory depression, decreased muscle tone and poor feeding (floppy infant syndrome).

Do not breast-feed while taking Alprazolam Krka. There is a risk of an effect on the baby.

Driving and using machines
Because of its sedative, muscle relaxing and drowsiness-inducing effect, alprazolam may impair performance in traffic and in other tasks requiring special alertness, especially at the beginning of treatment and if insufficient sleep. For this reason, do not drive or operate machines during treatment with Alprazolam Krka.

Alprazolam Krka contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Alprazolam Krka

Your doctor has prescribed an individual dosage and duration of therapy suited to your condition. Always take Alprazolam Krka exactly as your doctor has told you. Treatment is often started with a low dose, which is gradually increased as necessary. Do not change the dosage or stop taking Alprazolam Krka without talking to your doctor. It is recommended that the doctor prescribing, monitoring and stopping the treatment be the same oneDo not pass Alprazolam Krka tablets to others.

Please note that Alprazolam Krka prolonged-release tablets should be swallowed whole, they should not be divided or crushed!

Treatment duration
The risk of dependency and abuse may increase with the dose and duration of treatment. The doctor will therefore prescribe the lowest effective dose and treatment duration possible, and frequently reassess the need for continued treatment (see section 2 - Warnings and precautions).

The maximum duration of treatment should not be more than 2-4 weeks. Long-term treatment is not recommended.

Anxiety:
The initial dose is usually 0.5 mg once daily. The therapeutic dose is generally 0.5–3 mg daily, taken in one or divided in two doses. Lower initial and therapeutic doses are recommended for elderly or debilitated patients, a maximum of 0.5 - 1 mg per day.

Use in children and adolescents
The safety and efficacy of alprazolam in patients under 18 years old have not been established. Therefore, use of alprazolam is not recommended in this age group.

If you take more Alprazolam Krka than you should
If you take, or if someone else (e.g. a child) takes, too large dose of the medicine, immediately contact your doctor or a hospital. Activated charcoal should be given as emergency medication if the patient is conscious.

Take this carton with you if you seek medical help.

An overdose of alprazolam causes heavy fatigue, ataxia (incoordination) and a reduced level of consciousness. Lowering of blood pressure, unconsciousness and respiratory depression are also possible. Alcohol and other central nervous system depressants increase the undesirable effects of alprazolam.

If you forget to take Alprazolam Krka
Take the forgotten dose as soon as possible. If it is close to the time of your next dose, do not take the missed dose. Never take a double dose or two doses in rapid succession. Before going on holiday or taking a trip, ensure that you take enough Alprazolam Krka with you.

If you stop taking Alprazolam Krka
Always ask your doctor before you stop taking Alprazolam Krka as the dose needs to be reduced gradually.
Alprazolam may cause physical and psychic dependence. The risk is greatest with high doses and long treatment periods, in patients with history of alcohol or drug abuse or if several benzodiazepines are combined.
Abruptly stopping treatment causes withdrawal symptoms (e.g. headache, muscle pain, severe anxiety, tension, restlessness, confusion, irritability and in severe cases depersonalisation, derealisation, hyperacusis, numbness, tingling sensations in the limbs, hypersensitivity to light, noice and touch, hallucinations and epileptic seizures). Withrawal symptoms can appear several days after the end of treatment.

For this reason, **Alprazolam Krka therapy must not be terminated abruptly**; the dose should be reduced gradually according to the instructions of your doctor.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

You should stop taking Alprazolam Krka and contact a doctor immediately if you experience symptoms of angioedema (frequency is not known), such as
- swollen face, tongue or throat,
- difficulty to swallow,
- hives and difficulties to breath.

Stop taking Alprazolam Krka and contact your doctor as soon as possible if you get any of the following symptoms **:**
- Yellowing of the skin and whites of the eyes (jaundice).
- Reactions such as agitation, restlessness, aggressiveness, irritability, violent anger, false beliefs, nightmares and hallucinations or mental illness that characterized by distorted perception of reality (psychosis), inappropriate behavior and others behavioral disorders. These reactions occur more frequently in elderly patients.
- Depression/depressive thoughts.

Other possible side effects that may occur are:
Very common effects *(may affect more than 1 in 10 people)*:
- depression, sedation, sleepines and drowsiness, ataxia (incoordination), memory impairment, speech difficulties, dizziness, headache
- constipation, dry mouth
- tiredness, irritability.

Common side effects *(may affect up to 1 in 10 people)*:
- decreased appetite, increased appetite
- confusion, disorientation, changes in sexual drive (libido decreased, libido increased), anxiety, insomnia, nervousness
- balance disorder, coordination dificulties, concentration difficulties, inability to stay awake, feeling sluggish, tremor (shaking)

- blurred vision
- nausea, vomiting
- skin inflamation (dermatitis)
- sexual dysfunction
- weight change

Uncommon side effects *(may affect up ti 1 in 100 people)*:
- elevated mood (mania), hallucinations, rage, agitation, drug dependence
- amnesia (loss of memory), feeling of intoxication
- muscle weakness
- incontinence, menstrual irregularities

Not known *(frequency cannot be estimated from the available data)*:
- overproduction of the hormone prolactin
- elevated mood (hypomania), aggressive or hostile behaviour, abnormal thoughts (delusion), being hyperactive, drug abuse (see section 2 “Warnings and precautions”)
- nervous system imbalance (palpitations, increased salivary production, nasal congestion), reduced alertness, difficulties in speeking, twisting or jerky movenemts (dystonia)
- gastrointestinal disorder, swallowing difficulty
- inflamation of the liver (hepatitis), yelowing of the skin and whites of the eye (jaundice), abnormal liver function
- skin reaction caused by sensitivity to sunlight
- difficulty urinating
- peripheral oedema
- increased pressure in the eyes.

Alprazolam may cause physical and psychic dependence. See section “Warnings and precautions”.

Abrupt termination of Alprazolam Krka therapy may cause withdrawal symptoms such as anxiety, sleeplessness and convulsions (see 'If you stop taking Alprazolam Krka tablets’).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Alprazolam Krka

Keep this medicine out of the sight and reach of children.

This medicinal product does not require any special storage conditions.

Do not use this medicine after the expiry date which is stated on the carton and the blister after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Alprazolam Krka contains

- The active substance is alprazolam. Each prolonged-release tablet contains 0.5 mg, 1 mg or 2 mg alprazolam.
- The other ingredients are lactose monohydrate, hypromellose, magnesium stearate, indigo carmine (E132) (only in 0.5 mg and 2 mg tablets), quinoline yellow (E104) (only in 0.5 mg tablets). See section 2: “Alprazolam Krka contains lactose”.

What Alprazolam Krka looks like and contents of the pack
Alprazolam Krka 0.5 mg: greenish-yellow, round, slightly biconvex.
Alprazolam Krka 1 mg: white, round, slightly biconvex.
Alprazolam Krka 2 mg: light blue, round, slightly biconvex.

Pack sizes: 20, 30, 60, 100 and 100x1 prolonged-release tablets
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:

[To be completed nationally]

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Detailed information on this medicine is available on the website of {name of Member State Agency (link)}