Package leaflet: Information for the patient

Tramadol Krka 50 mg hard capsules
tramadol hydrochloride

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

Tramadol – the active substance in Tramadol Krka – is a painkiller belonging to the class of opioids that acts on the central nervous system. It relieves pain by acting on specific nerve cells of the spinal cord and brain.

Tramadol Krka capsules are used for the treatment of moderate to severe pain in adults and children aged 12 years and over.

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

Do not take Tramadol Krka
- if you are allergic to tramadol or any of the other ingredients of this medicine (listed in section 6);
- in acute poisoning with alcohol, sleeping pills, pain relievers or other medicines that affect mood and emotions;
- if you are also taking MAO inhibitors (certain medicines used for treatment of depression) or have taken them in the last 14 days before treatment with Tramadol Krka (see "Other medicines and Tramadol Krka");
- if you suffer from epilepsy and your fits are not adequately controlled by treatment;
- as a substitute in drug withdrawal.

Warnings and precautions
Talk to your doctor or pharmacist before taking Tramadol Krka:
- if you think that you are addicted to other pain relievers (opioids);
- if you suffer from consciousness disorders (if you feel that you are going to faint);
- if you are in a state of shock (cold sweat may be a sign of this);
- if you suffer from increased pressure in the brain (possibly after a head injury or brain disease);
- if you have difficulty in breathing;
- if you have a tendency towards epilepsy or fits because the risk of a fit may increase;
- if you suffer from a liver or kidney disease;
- if you suffer from depression and you are taking antidepressants as some of them may interact

with tramadol (see "Other medicines and Tramadol Krka ").

Serotonin syndrome
There is a small risk that you may experience a so-called serotonin syndrome that can occur after having taken tramadol in combination with certain antidepressants or tramadol alone. Seek medical advice immediately if you have any of the symptoms related to this serious syndrome (see section 4 "Possible side effects").

Sleep-related breathing disorders
Tramadol Krka can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

Epileptic fits have been reported in patients taking tramadol at the recommended dose level. The risk may be increased when doses of tramadol exceed the recommended upper daily dose limit (400 mg).

Tolerance, dependence, and addiction
This medicine contains tramadol which is an opioid medicine. Repeated use of opioids can result in the drug being less effective (you become accustomed to it, known as tolerance). Repeated use of Tramadol Krka can also lead to dependence, abuse and addiction, which may result in life-threatening overdose. The risk of these side effects can increase with a higher dose and longer duration of use.

Dependence or addiction can make you feel that you are no longer in control of how much medicine you need to take or how often you need to take it.

The risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent on or addicted to Tramadol Krka if:
- You or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs (“addiction”).
- You are a smoker.
- You have ever had problems with your mood (depression, anxiety, or a personality disorder) or have been treated by a psychiatrist for other mental illnesses.

If you notice any of the following signs whilst taking Tramadol Krka, it could be a sign that you have become dependent or addicted:
- You need to take the medicine for longer than advised by your doctor
- You need to take more than the recommended dose
- You are using the medicine for reasons other than prescribed, for instance, ‘to stay calm’ or ‘help you sleep’
- You have made repeated, unsuccessful attempts to quit or control the use of the medicine
- When you stop taking the medicine you feel unwell, and you feel better once taking the medicine again (‘withdrawal effects’)

If you notice any of these signs, speak to your doctor to discuss the best treatment pathway for you, including when it is appropriate to stop and how to stop safely (See section 3, If you stop taking Tramadol Krka).

Please also inform your doctor if one of these problems occurs during Tramadol Krka treatment or if they applied to you in the past.

Talk to your doctor if you experience any of the following symptoms while taking Tramadol Krka: Extreme fatigue, lack of appetite, severe abdominal pain, nausea, vomiting or low blood pressure. This may indicate that you have adrenal insufficiency (low cortisol levels). If you have these symptoms, contact your doctor, who will decide if you need to take hormone supplement.

Tramadol is transformed in the liver by an enzyme. Some people have a variation of this enzyme and this can affect people in different ways. In some people, they may not get enough pain relief but other people are more likely to get serious side effects. If you notice any of the following side effects, you must stop taking this medicine and seek immediate medical advice: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation, lack of appetite.

Children and adolescents

Use in children with breathing problems
Tramadol is not recommended in children with breathing problems, since the symptoms of tramadol toxicity may be worse in these children.

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

Tramadol Krka should not be taken together with MAO inhibitors (certain medicines for the treatment of depression).

The pain-relieving effect of Tramadol Krka may be reduced and the length of time it acts may be shortened, if you take medicines which contain
- carbamazepine (for epileptic fits);
- ondansetron (prevents nausea).

Your doctor will tell you whether you should take Tramadol Krka, and which dose.

Concomitant use of Tramadol Krka and sedative medicines such as benzodiazepines or related drugs 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 Tramadol Krka together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.
Please tell your doctor about all sedative 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 risk of side effects increases,
- if you are taking sleeping pills, other pain relievers such as morphine and codeine (also as cough medicine), and alcohol while you are taking Tramadol Krka. You may feel drowsier or feel that you might faint. If this happens tell your doctor.
- if you are taking medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk having a fit may increase if you take Tramadol Krka at the same time. Your doctor will tell you whether Tramadol Krka is suitable for you.
- if you are taking certain antidepressants, Tramadol Krka may interact with these medicines and you may experience serotonin syndrome (see section 4 "Possible side effects").
- if you are taking coumarin anticoagulants (medicines that prevent blood clotting), e.g. warfarin, together with Tramadol Krka. The effect of these medicines on blood clotting may be affected and bleeding may occur.
- if you are taking gabapentin or pregabalin to treat epilepsy or pain due to nerve problems (neuropathic pain).

Tramadol Krka with food and alcohol
Do not drink alcohol during treatment with Tramadol Krka as its effect may be intensified.
Food does not influence the effect of Tramadol Krka.

Pregnancy and breast-feeding and fertility
Pregnancy
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

There is very little information regarding the safety of tramadol during pregnancy in human. Therefore you should not use Tramadol Krka if you are pregnant.
Chronic use of Tramadol Krka during pregnancy may lead to tramadol dependance in the unborn child and consequently to withdrawal symptoms in newborns.

Breast-feeding
Tramadol is excreted into breast milk. For this reason, you should not take Tramadol Krka more than once during breast-feeding, or alternatively, if you take Tramadol Krka more than once, you should stop breast-feeding.

Fertility
Based on human experience tramadol is suggested not to influence female or male fertility.

Driving and using machines
Tramadol Krka may cause drowsiness, dizziness and visual disturbances (blurred vision) and therefore may impair your reactions. If you feel that your reactions are affected, do not drive a car or other vehicle, do not use electric tools or operate machinery.

Tramadol Krka contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Tramadol Krka

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using Tramadol Krka, when and how long you need to take it, when to contact your doctor, and when you need to stop it (see also section 2).

The dosage should be adjusted to the intensity of your pain and your individual pain sensitivity. In general the lowest pain-relieving dose should be taken. Do not take more than 8 capsules of Tramadol Krka daily (which is equivalent to 400 mg tramadol hydrochloride), except if your doctor has instructed you to do so.

Unless otherwise prescribed by your doctor, the usual dose is:

<u>Adults and adolescents from the age of 12 years</u>
The usual dose is 1 or 2 capsules every 4-6 hours.

The recommended dose for moderate pain is 1 hard capsule of Tramadol Krka (corresponding to 50 mg tramadol hydrochloride). If no pain relief occurs within 30 to 60 minutes, a second capsule can be taken.

A higher demand for pain relief may be expected for severe pain, in this case 2 hard capsules can be taken as a single dose of Tramadol Krka (corresponding to 100 mg of tramadol hydrochloride).

<u>Children</u>
Tramadol Krka capsules are not suitable for children below the age of 12 years.

Elderly patients
In elderly patients (above 75 years) the excretion of tramadol may be delayed. If this applies to you, your doctor may recommend prolonging the dosage interval.

Severe liver or kidney disease (insufficiency)/dialysis patients
Patients with severe liver and/or kidney insufficiency should not take Tramadol Krka. If in your case the insufficiency is mild or moderate, your doctor may recommend prolonging the dosage interval.

How and when should you take Tramadol Krka?
Tramadol Krka are for oral use.

Always swallow Tramadol Krka whole, not divided or chewed, with sufficient liquid. You may take the capsule on an empty stomach or with meals.

How long should you take Tramadol Krka?
You should not take Tramadol Krka longer than necessary. If you need to be treated for a longer period, your doctor will check at regular, short intervals (if necessary with breaks in treatment) whether you should continue taking Tramadol Krka and at what dose.

Please talk to your doctor or pharmacist if you have the impression that the effect of Tramadol Krka is too strong or too weak.

If you take more Tramadol Krka than you should
If you have taken an additional dose of Tramadol Krka by mistake, this will generally have no negative effects. You should take your next dose as prescribed.

If you (or someone else) swallow a lot of Tramadol Krka capsules at the same time you should go to hospital or call a doctor straight away. Signs of an overdose include very small pupils, vomiting, fall in blood pressure, rapid heartbeat, circulatory collapse, unconsciousness up to coma (deep unconsciousness), fits and breathing difficulties or shallow breathing up to respiratory arrest. If these signs occur, contact your doctor immediately.

If you forget to take Tramadol Krka
If you forget to take Tramadol Krka capsules, pain is likely to return. Do not take a double dose to make up for forgotten individual doses, simply continue taking the Tramadol Krka capsules as before.

If you stop taking Tramadol Krka
If you interrupt or finish treatment with Tramadol Krka too soon, pain is likely to return. If you wish to stop treatment on account of unpleasant effects, please tell your doctor.

You should not suddenly stop taking this medicine unless your doctor tells you to. If you want to stop taking your medicine, discuss this with your doctor first, particularly if you have been taking it for a long time. Your doctor will advise you when and how to stop, which may be by lowering the dose gradually to reduce the chance of developing unnecessary side effects (withdrawal symptoms).

Generally there will be no after-effects when treatment with Tramadol Krka is stopped. However, on rare occasions, people who have been taking Tramadol Krka for some time may feel unwell if they abruptly stop taking them. They may feel agitated, anxious, nervous or shaky. They may be hyperactive, have difficulty sleeping and have stomach or bowel disorders. Very few people may get panic attacks, hallucination, unusual perceptions such as itching, tingling and numbness, and "ringing" in the ears (tinnitus). Further unusual CNS symptoms, i.e. confusion, delusions, change of perception of the own personality (depersonalisation), and change in perception of reality (derealisation) and delusion of persecution (paranoia) have been seen very rarely. If you experience any of these complaints after stopping Tramadol Krka, please consult your doctor.

If you have any further questions on the use of this medicine, 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 see a doctor immediately if you experience symptoms of an allergic reaction such as swollen face, tongue and/or throat, and/or difficulty swallowing or hives together with difficulties in breathing.

Very common (may affect more than 1 in 10 people)
- dizziness
- feeling sick (nausea)

Common (may affect up to 1 in 10 people)
- headaches, drowsiness
- tiredness
- constipation, dry mouth, vomiting
- excessive sweating (hyperhidrosis)

Uncommon (may affect up to 1 in 100 people)
- effects on the heart and blood circulation (pounding of the heart, fast heartbeat (tachycardia), dizzy spells (orthostatic hypotension or circulatory collapse). These adverse effects may particularly occur in patients when standing up and in patients under physical strain
- urge to be sick (retching), stomach trouble (e.g. feeling of pressure in the stomach, bloating), diarrhoea
- skin reactions (e.g. itching, rash)

Rare (may affect up to 1 in 1,000 people)
- allergic reactions (e.g. difficulty breathing (dyspnoea), wheezing, water retention in tissues (angioedemal) and shock reactions (sudden circulation failure) occur very rarely
- slow heartbeat (bradycardia)
- increase in blood pressure
- abnormal skin sensations (e.g. itching, tingling, numbness), trembling (tremor), involuntary muscle twitching, uncoordinated movement, transient loss of consciousness (syncope), speech disorders
- Epileptic fits have occurred mainly at high doses of tramadol or when tramadol was taken at the same time as other medicines which may induce fits
- changes in appetite
- hallucination, confusion, sleep disorders, anxiety and nightmares
- Psychological complaints may appear after treatment with Tramadol Krka. Their intensity and nature may vary (according to the patient's personality and length of therapy). These may appear as a change in mood (mostly high spirits, occasionally irritated mood), changes in activity (usually suppression, occasionally increase) and decreased cognitive and sensory perception (being less aware and less able to make decisions, which may lead to errors in judgement)
- Drug dependence may occur.When treatment is stopped abruptly, signs of withdrawal may appear (see "If you stop taking Tramadol Krka")
- blurred vision, excessive dilation of the pupils (mydriasis), narrow pupils (miosis)
- slow breathing (respiratory depression), shortness of breath (dyspnoea)
- Worsening of asthma has been reported, however it has not been established whether it was caused by tramadol. If the recommended doses are exceeded, or if other medicines that depress brain function are taken at the same time, breathing may slow down
- weak muscles
- passing urine with difficulty or pain, passing less urine than normal (micturition disorders and dysuria)

Very rare (may affect up to 1 in 10,000 people)
- increased hepatic enzyme

Not known (frequency cannot be estimated from the available data)
- decrease in blood sugar level
- hiccups
- serotonin syndrome, that can manifest as mental status changes (e.g. agitation, hallucinations, coma), and other effects, such as fever, increase in heart rate, unstable blood pressure, involuntary twitching, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea) (see section 2 "What you need to know before you take Tramadol Krka ")

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 HPRA Pharmacovigilance. Website: www.hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Tramadol Krka

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

Store this medicine in a safe and secure storage space, where other people cannot access it. It can cause serious harm and be fatal to people when it has not been prescribed for them.

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

Do not store above 30°C.
Store in the original package in order to protect from moisture.

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 Tramadol Krka contains
- The active substance is tramadol hydrochloride. Each hard capsule contains 50 mg tramadol hydrochloride.
- The other ingredients (excipients) are microcrystalline cellulose, sodium starch glycolate (type A), talc and magnesium stearate (E470b) in the capsule core and titanium dioxide (E171), indigo carmine (E132) and gelatin in the capsule shell.

What Tramadol Krka looks like and contents of the pack
Hard capsules (capsules): the body of the capsule is white and the cap is blue. Capsules are filled with white or almost white powder. The size of the capsule is No: 4. The length of filled capsules is 14-15 mm.

Tramadol Krka is available in boxes containing 10, 20, 30, 50, 60, 90 and 100 hard capsules in blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Krka, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Name of the member state	Name of the medicine
Croatia	Awardix
Belgium, Bolgaria, Czech Republic, Denmark, Poland, Hungary, Ireland, United Kingdom (Northern Ireland), Spain, Portugal, Slovakia, Sweden	Tramadol Krka
Italy	Tramadolo Krka

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