Package leaflet: Information for the patient

Tramadol/Paracetamol Krka 37.5 mg/325 mg film-coated tablets
tramadol hydrochloride/paracetamol

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

What is in this leaflet

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

Tramadol/Paracetamol Krka is a combination of two analgesics (pain killers) tramadol and paracetamol that act together to relieve your pain.
Tramadol/Paracetamol Krka is intended for use in the treatment of moderate to severe pain when your doctor recommends that a combination of tramadol and paracetamol is needed.

Tramadol/Paracetamol Krka should only be taken by adults and adolescents over 12 years.

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

Do not take Tramadol/Paracetamol Krka if you
- are allergic to paracetamol, tramadol or any of the other ingredients of this medicine (listed in section 6)
- are in acute poisoning with alcohol, sleeping pills, pain relievers or other psychotropic medicines (medicines that affect mood and emotions)
- are also taking MAO inhibitors (certain medicines used for treatment of depression or Parkinson's disease) or have taken them in the last 14 days before treatment with Tramadol/Paracetamol Krka
- suffer from severe liver problems
- have epilepsy that is not adequately controlled on your current medicine.

Warnings and precautions
Talk to your doctor or pharmacist before taking Tramadol/Paracetamol Krka.
Take special care with Tramadol/Paracetamol Krka if you:
- have kidney problems
- have liver problems or alcoholic liver disease or you have noticed your eyes and skin turning yellow, which may suggest jaundice or problems with bile ducts
- have difficulty breathing, for example, asthma or lung problems
- are dependent on any other medicines used to relieve moderate to severe pain, for example, morphine
- are epileptic or if have you experienced fits or seizures

- have suffered from a head injury, shock or severe headaches which may or may not be associated with vomiting
- take other medicines containing paracetamol or tramadol
- take other medicines to treat pain that contain buprenorphine, nalbuphine or pentazocine;
- are going to have an anaesthetic. Tell your doctor or dentist that you are taking Tramadol/Paracetamol Krka.
- if you suffer from depression and you are taking antidepressants as some of them may interact with tramadol (see "Other medicines and Tramadol/Paracetamol 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.

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/Paracetamol 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.

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

Important: This medicine contains paracetamol and tramadol. Tell your doctor if you are taking any other medicine containing paracetamol or tramadol, so that you do not exceed the maximum daily doses.

You **must not** take Tramadol/Paracetamol Krka together with monoamine oxidase inhibitors ("MAOIs") (see section "Do not take Tramadol/Paracetamol Krka").

Tramadol/Paracetamol Krka is not recommended with the following medicines, as it may affect how well they work:
- carbamazepine (a medicine used to treat epilepsy or some types of pain)
- buprenorphine, nalbuphine or pentazocine (opioid-type pain relievers). The pain-relieving effect may be reduced.

Tramadol/Paracetamol Krka may increase the risk of side effects if you also take the following medicines:

- triptans (used for migraine) or selective serotonin re-uptake inhibitors (SSRIs, used for depression). Check with your doctor if you experience confusion, restlessness, fever, sweating, uncoordinated movement of limbs or eyes, uncontrollable jerking of muscles or diarrhoea.
- tranquilizers, sleeping pills, other pain relievers such as morphine and codeine (also as cough medicine), baclofen (a muscle relaxant), medicines used to lower blood pressure, antidepressants or medicines to treat allergies. Check with your doctor if you feel drowsy or feel faint.
- medicines which may cause convulsions (fits), such as certain antidepressants, antipsychotics, anaesthetics, medicines that affect the state of mind, or bupropion (used to help stop smoking). The risk of having a fit may increase if you take Tramadol/Paracetamol Krka at the same time. Your doctor will tell you whether Tramadol/Paracetamol Krka is suitable for you.
- certain antidepressants. Tramadol/Paracetamol Krka may interact with these medicines and you may experience serotonin syndrome (see section 4 "Possible side effects").
- warfarin or phenprocoumon (for blood thinning). The effectiveness of such medicines may be altered and bleeding may occur (see section 4). Any prolonged or unexpected bleeding should be reported to your doctor immediately.
- flucloxacillin (antibiotic), due to a serious risk of blood and fluid abnormality (high anion gap metabolic acidosis) that must have urgent treatment and which may occur particularly in case of severe renal impairment, sepsis (when bacteria and their toxins circulate in the blood leading to organ damage), malnutrition, chronic alcoholism, and if the maximum daily doses of paracetamol are used.

The effectiveness of Tramadol/Paracetamol Krka may be altered if you also take the following medicines:
- metoclopramide, domperidone or ondansetron (medicines used to treat nausea and vomiting/being sick)
- cholestyramine (medicine used to reduce cholesterol in the blood).

Concomitant use of Tramadol/Paracetamol 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/Paracetamol 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.

Tramadol/Paracetamol Krka with food, drink and alcohol
Tramadol/Paracetamol Krka can be taken with or without food.
- Tramadol/Paracetamol Krka may make you feel drowsy. Alcohol may make you feel drowsier. Alcohol: increases the sedative effect of opioid analgesics, the effect on alertness can make driving of vehicles and the use of machines dangerous, avoid intake of alcoholic drinks and of medicinal products containing alcohol.

Pregnancy, breast-feeding and fertility
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.

Pregnancy
Since Tramadol/Paracetamol Krka is a fixed combination of active ingredients including tramadol, it should not be used during pregnancy.

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

more than once, you should stop breast-feeding.

Fertility
Based on human experience tramadol is suggested not to influence female or male fertility. No data on the influence of the combination of tramadol and paracetamol on fertility are available.

Driving and using machines
Do not drive, operate machinery or perform other activities for which you need to be alert until you know how Tramadol/Paracetamol Krka affects you. Tramadol/Paracetamol Krka may make you feel drowsy.

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

3. How to take Tramadol/Paracetamol Krka

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

The usual starting dose is two tablets. If required, further doses can be taken after every six hours, as recommended by your doctor.
Do not take more than 8 tablets per day (equivalent to 300 mg tramadol hydrochloride and 2600 mg paracetamol).
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.

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

Use in children
Tramadol/Paracetamol Krka is not recommended for use in children under 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.

Method of administration
The tablets must be swallowed with some liquid. The tablets should not be chewed or crushed.
The tablets should be taken for as short a time as possible.
If you think that the effect of Tramadol/Paracetamol Krka is too strong (i.e. you feel very drowsy or have difficulty with breathing) or too weak (i.e. you have inadequate pain relief), contact your doctor or pharmacist. If your symptoms do not get any better, see your doctor.

If you take more Tramadol/Paracetamol Krka than you should
Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage. If you take more Tramadol/Paracetamol Krka than you should you could experience severe disturbance of blood supply to organs, consciousness disorders up to coma, convulsions, or you might have difficulty breathing, feel unwell, vomit, lose weight or feel abdominal pain.

If you forget to take Tramadol/Paracetamol Krka
Do not take a double dose to make up for a forgotten tablet.

If you miss a dose of Tramadol/Paracetamol Krka, take your next tablet at the usual time.

If you stop taking Tramadol/Paracetamol Krka
If you have been using Tramadol/Paracetamol Krka for some time, you should talk to your doctor if you want to stop because your body may have got used to it. 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). If you do suddenly stop using Tramadol/Paracetamol Krka you may feel unwell. You may experience anxiety, agitation, nervousness, sleeplessness, hyperactivity, tremors and/or an upset stomach.

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.

The very common side effects (may affect more than 1 in 10 people):
- nausea,
- dizziness,
- drowsiness.

These are usually mild and not troublesome.

Common side effects (may affect up to 1 in 10 people):
- vomiting,
- digestion problems (constipation, flatulence, diarrhoea),
- stomach pain,
- dry mouth,
- headache,
- shaking,
- confusion,
- sleep disorders,
- mood changes (anxiety, nervousness, euphoria (a sense of feeling "high" all the time)),
- increased sweating,
- itching.

Uncommon side effects (may affect up to 1 in 100 people):
- high blood pressure, heart rhythm and heart rate disorders,
- difficulty or pain on passing urine, protein in the urine,
- skin reactions (hives, rashes),
- ringing in the ear,
- depression,
- nightmares,
- hallucinations (hearing, seeing or sensing things that are not really there),
- loss of memory,
- difficulty swallowing,
- blood in the stools,
- shivering,
- hot flushes,
- pain in the chest,
- involuntary muscle twitching,
- unusual tingling feeling ("pins and needles"),
- shortness of breath,
- raised liver enzymes.

Rare side effects (may affect up to 1 in 1,000 people):
- drug dependence,
- fits, difficulties in carrying out coordinated movements,
- blurred vision,
- acute confusional state (delirium),
- transient loss of consciousness,
- constriction of the pupil (miosis),
- speech disorders,
- excessive dilation of the pupils (mydriasis).

Very rare side effect (may affect up to 1 in 10,000 people):
- drug abuse.

Unknown side effect (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/Paracetamol Krka").

The following are recognised side effects which have been reported by people using medicines that contain only tramadol hydrochloride or paracetamol. However, if you experience any of these while taking Tramadol/Paracetamol Krka, you should tell your doctor:
- feeling faint when getting up from a lying or sitting position, slow heart rate, fainting, changes in appetite, muscle weakness, slower or weaker breathing, mood changes, changes in activitiy, changes in perception, worsening of asthma.
- in some rare cases a skin rash, indicating an allergic reaction, may develop with sudden swelling of the face and neck, difficulties breathing or drop of blood pressure and fainting. If this happens to you, stop treatment and see a doctor immediately. You must not take the medicine again.

On rare occasions, people who have been taking tramadol for some time may feel unwell if they stop treatment abruptly. 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 also get panic attacks, hallucinations, unusual perception such as itching, tingling, numbness and ringing in the ears (tinnitus). If you do notice any of these effects, or any other unusual symptoms, please tell your doctor or pharmacist as soon as possible.
In exceptional cases blood tests may reveal certain abnormalities, for instance, low counts of blood platelets, which may result in nose bleeds or bleeding gums.
Very rare cases of serious skin reactions have been reported for paracetamol containing medicines.

Use of Tramadol/Paracetamol Krka together with medicines used to thin the blood (e.g. phenoprocoumon, warfarin) may increase the bleeding risk. Any prolonged or unexpected bleeding should be reported to your doctor immediately.

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/Paracetamol Krka

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

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.

This medicine does not require any special storage conditions.

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/Paracetamol Krka contains
- The active substances are tramadol hydrochloride and paracetamol. Each film-coated tablet contains 37.5 mg mg tramadol hydrochloride equivalent to 32.94 mg tramadol and 325 mg paracetamol.
- The other ingredients are:
  - *Tablet core:* pregelatinised maize starch, sodium starch glycolate (type A), microcrystalline cellulose (E460) and magnesium stearate (E470b).
  - *Film-coating:* hypromellose, titanium dioxide (E171), macrogol 400, yellow iron oxide (E172) and polysorbate 80.

  See section 2 "Tramadol/Paracetamol Krka contains sodium".

What Tramadol/Paracetamol Krka looks like and contents of the pack
Film-coated tablets are yellow-brown, oval, slightly biconvex.
Boxes of 2 film-coated tablets (blisters with 2 tablets) or 10, 20, 30, 40, 50, 60, 70, 80, 90 and 100 film-coated tablets (blisters with 10 tablets) are available.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

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

Czech Republic, Hungary, Latvia, Lithuania, Poland, Romania, Slovak Republic, Slovenia, Bulgaria, Estonia	Doreta
Germany	Tramabian
France	TRAMADOL/PARACETAMOL KRKA
Spain, Ireland, Austria, Belgium, The Netherlands	Tramadol/Paracetamol Krka
Italy	Tramadolo e Paracetamolo Krka
United Kingdom	Tramadol Hydrochloride/Paracetamol

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