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 tramadol and paracetamol, which 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 tramadol hydrochloride, paracetamol 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 a severe liver disorder
- have epilepsy that is not adequately controlled on your current medicine.

Warnings and precautions
Talk to your doctor before taking Tramadol/Paracetamol Krka if you:
- take other medicines containing paracetamol or tramadol
- have liver problems or liver disease or if you notice your eyes and skin turning yellow. This may suggest jaundice or problems with your bile ducts
- have kidney problems
- have severe difficulties in breathing for example asthma or severe lung problems
- have epilepsy or have already experienced fits or seizures
- 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")

- have recently suffered from a head injury, shock or severe headaches associated with vomiting
- are dependent on any medicines including those used to relieve pain, for example, morphine
- 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.

Sleep-related breathing disorders
Tramadol/Paracetamol Krka contains an active substance that belongs to the group of opioids. Opioids can cause sleep- related breathing disorders, for example central sleep apnea (shallow/pause of breathing during sleep) and sleep-related hypoxemia (low level of oxygen in the blood).
The risk of experiencing central sleep apnea is dependent on the dose of opioids. Your doctor may consider decreasing your total opioid dosage if you experience central sleep apnea.

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").

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.

If any of the above-mentioned points applied to you in the past or applies to you while you are taking Tramadol/Paracetamol Krka, please make sure your doctor knows. He/she can then decide whether you should continue to use this medicine.

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.

Talk to your doctor if you experience any of the following symptoms while taking 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.

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 to be taken with the following:*
- carbamazepine (a medicine commonly used to treat epilepsy or some types of pain such as severe pain attacks in the face called trigeminal neuralgia).
- buprenorphine, nalbuphine or pentazocine (opioid-type pain relievers). The pain-relieving effect may be reduced.

Please inform your doctor or pharmacist if you are taking:

- flucloxacillin (antibiotic), due to a serious risk of blood and fluid abnormality (high anion gap metabolic acidosis which occurs when there is an increase in blood plasma acidity) that must have urgent treatment and which may occur particularly in case of severe kidney or liver 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, especially if you take the maximum daily dose of paracetamol for longer time. High anion gap metabolic acidosis is a serious disease that must have urgent treatment.

The risk of side effects increases, if you are taking:

- triptans (for migraine) or selective serotonin re-uptake inhibitors, "SSRIs" (for depression). If you experience confusion, restlessness, fever, sweating, uncoordinated movement of limbs or eyes, uncontrollable jerking of muscles or diarrhoea you should call your doctor.
- other pain relievers such as morphine and codeine (also as cough medicine), baclofen (a muscle relaxant) medicines used to lower blood pressure or medicines to treat allergies. You may feel drowsy or feel faint. If this happens, tell your doctor.
  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 prescribes 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.
- medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk 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. Any prolonged or unexpected bleeding should be reported to your doctor immediately.

The effectiveness of Tramadol/Paracetamol Krka may be altered if you also take:

- metoclopramide, domperidone or ondansetron (medicines for treatment of nausea and vomiting),
- cholestyramine (medicine to reduce cholesterol in the blood).

Your doctor will tell you which medicines are safe to take with Tramadol/Paracetamol Krka.

Tramadol/Paracetamol Krka with food and alcohol

Tramadol/Paracetamol Krka may make you feel drowsy. Alcohol may make you feel drowsier, so it is best not to drink alcohol while you are taking Tramadol/Paracetamol Krka.

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.

As Tramadol/Paracetamol Krka contains tramadol, you should not take this medicine during pregnancy or breast-feeding. If you become pregnant during treatment with Tramadol/Paracetamol Krka please consult your doctor before taking any further tablets.

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.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Tramadol/Paracetamol Krka may make you feel drowsy and this may affect your ability to drive, or use tools and machines, safely.

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.

You should take Tramadol/Paracetamol Krka for as short a time as possible.
The use in children below the age of 12 years is not recommended.

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.

The recommended starting dose, unless otherwise prescribed by your doctor, is 2 tablets for adults and adolescents over 12 years.

If required, further doses may be taken, as recommended by your doctor. The shortest time between doses must be at least 6 hours.

Do not take more than 8 Tramadol/Paracetamol Krka film-coated tablets per day.
Do not take Tramadol/Paracetamol Krka more often than your doctor has told you.

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/Paracetamol Krka.
If in your case the insufficiency is mild or moderate, your doctor may recommend prolonging the dosage interval.

Method of administration
The tablets are for oral use.
Swallow the tablets whole with sufficient liquid. They should not be broken or chewed.

If you think that the effect of Tramadol/Paracetamol Krka is too strong (i.e. you feel very drowsy or have difficulty breathing) or too weak (i.e. you have inadequate pain relief), contact your doctor.

If you take more Tramadol/Paracetamol Krka than you should
In such cases please contact your doctor or pharmacist immediately even if you feel well. There is a

risk of liver damage which may only show later.

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

If you stop taking Tramadol/Paracetamol Krka
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 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.

Very common (may affect more than 1 in 10 people):
- nausea,
- dizziness, drowsiness.

Common (may affect up to 1 in 10 people):
- vomiting, digestion problems (constipation, flatulence, diarrhoea), stomach pain, dry mouth,
- itching, sweating (hyperhidrosis),
- headache, shaking,
- confusional state, sleep disorders, mood changes (anxiety, nervousness, a feeling of high spirits),

Uncommon (may affect up to 1 in 100 people):
- increase in pulse or blood pressure, heart rate or heart rhythm disorders,
- tingling, numbness or feeling of pins and needles in the limbs, ringing in the ear, involuntary muscle twitching,
- depression, nightmares, hallucination (hearing, seeing or sensing things that are not really there), memory lapses,
- difficulty breathing,
- difficulty swallowing, blood in the stools,
- skin reactions (for example rashes, hives),
- increase in liver enzyme values,
- presence of albumin in urine, difficulties or pain on passing urine,
- shivering, hot flushes, pain in the chest

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

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

Unknown (frequency not known):

- decrease in blood sugar level (hypoglycaemia).

The following are recognised side effects which have been reported by people using medicines that contain only tramadol or only 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 activity, changes in perception, worsening of existing asthma.
- paracetamol intake alone or when taken together with the antibiotic flucloxacillin may induce a blood and fluid abnormality (high anion gap metabolic acidosis) when there is an increase in blood plasma acidity.
- if you use Tramadol/Paracetamol Krka together with medicines used to thin the blood (e.g. phenprocoumon, warfarin) may increase the bleeding risk. Any prolonged or unexpected bleeding should be reported to your doctor immediately.
- 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.

In rare cases, using a medicine of the type of tramadol may make you become dependent on it, making it hard to stop taking it.
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 perceptions such as itching, tingling and numbness, and noise in the ears (tinnitus). If you experience any of these complaints after stopping Tramadol/Paracetamol Krka, please consult your doctor.
Frequency not known: 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").

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 with paracetamol.

Rare cases of respiratory depression have been reported with tramadol.

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 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
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

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 (Northern Ireland)	Tramadol hydrochloride/Paracetamol

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