Kalcex

Package leaflet: Information for the user

Tramadol 50 mg/ml solution for injection/infusion

Tramadol hydrochloride

Read all of this leaflet carefully before you start using 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 is and what it is used for

The active substance of Tramadol – tramadol hydrochloride (further in the text tramadol) – is opioid analgetic (painkiller) that acts on the central nervous system. It relieves pain due to its effect on specific nerve cells in the spinal cord and brain.

Tramadol is used to relieve moderate to severe pain.

2. What you need to know before you use Tramadol

Do not use Tramadol in the following cases:
- if you are allergic to tramadol or any of the ingredients of this medicine (listed in section 6);
- in acute intoxication with alcohol, sleeping pills, painkillers, opioids or other psychotropic medicines (medicines that affect mood and emotions);
- if you are taking or have taken in the last 14 days monoamine oxidase inhibitors (MAOIs) (medicines to treat depression) (see *Other medicines and Tramadol*);
- if you suffer from epilepsy and the treatment of seizures is not adequately controlled;
- as a drug substitute in the case of drug discontinuation.

Warnings and precautions
Talk to your doctor before you use Tramadol:
- if you think you are dependent on other painkillers (opioids);
- if you are hypersensitive to opiates;
- if you tend to be loss of consciousness (if you feel fainting);
- if you are in a state of shock (cold sweat may be a sign of this);
- if you suffer from elevated intracranial pressure (possible in the case of head injury or brain disease);
- if you have difficulty breathing;
- if you have a tendency towards epilepsy or fits because the risk of a fit may increase.

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.

Epileptic seizures are observed in patients taking tramadol at the recommended doses. The risk increases in excess of the maximum recommended daily dose of tramadol (400 mg).

Tramadol may cause psychological and physical dependence.

The long term use of Tramadol may reduce its efficacy, therefore you may need to use higher doses (addiction occurs). In patients prone to drug abuse or dependence, Tramadol should be used only for short periods and under strict medical supervision.

If during the treatment with Tramadol you experience any of mentioned problems or if you have experienced them before, please inform your doctor.

Children and adolescents
Tramadol should not be used in children under 1 year of age.

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
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Tramadol should not be used concomitantly with MAO inhibitors or within 14 days after their discontinuation (see *Do not use Tramadol in the following cases*).

The pain relief effect of Tramadol may be weakened and the duration of exposure shortened if you also take medicines containing:
- carbamazepine (used to treat epilepsy);
- ondansetron (prevents nausea).

Your doctor will tell you whether to use Tramadol and how large dose should be taken.

The risk of side effects increases:
- if you are taking tranquillizers, sleeping pills, other painkillers such as morphine or codeine (in cough medicines) and alcohol simultaneously with Tramadol. You may be feeling drowsy or feeling faint. If this happens, tell your nurse or doctor;
- if you are taking medicines that can cause fits, such as certain antidepressants. The risk of having a fit may increase if you take Tramadol at the same time. Your doctor will tell you whether Tramadol is suitable for you;
  - if you are taking certain antidepressants, Tramadol may interact with these medicines and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38 °C;
- if you are taking coumarin anticoagulants (medicines to thin the blood), such as warfarin, during the treatment with Tramadol. The effect of these medicines on blood clotting may be affected and bleeding may occur.

Tramadol with food and alcohol
Do not use alcohol during treatment with Tramadol because the activity of this medicine may be increased. Food doesn't affect the effectiveness of tramadol.

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.
Information on the safety of tramadol in pregnancy is very limited. Therefore, pregnant women should not take Tramadol.
Long-term treatment during pregnancy with Tramadol may result in withdrawal symptoms in newborns.
Tramadol is excreted into breast milk. For this reason, you should not take Tramadol Kalceks more than once during breast-feeding, or alternatively, if you take Tramadol Kalceks more than once, you should stop breast-feeding.
Postmarketing observations revealed no effects of tramadol on fertility. Animal studies have not detected tramadol effects on fertility.

Driving and using machines
Tramadol may cause drowsiness, dizziness and therefore affect your ability to react.
If you feel that your reaction is impaired, do not drive or operate machinery.
- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
  - The medicine has been prescribed to treat a medical or dental problem and
  - You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
  - It was not affecting your ability to drive safely.

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

3. How to use Tramadol

Always use Tramadol exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The dosage should be adjusted to the intensity of pain and individual pain sensitivity. In general the lowest pain-relieving dose should be taken. The total daily dose should not exceed 400 mg of tramadol (equivalent to 8 ml of Tramadol). In exceptional cases, if clinically necessary, your doctor may prescribe a higher daily dose.

Unless your doctor has prescribed otherwise, the usual dose is as follows.

Adults and adolescents aged over 12 years
Depending on the pain intensity 50–100 mg of tramadol is used every 4–6 hours. The maximum daily dose – 400 mg must not be exceeded.
Further information for healthcare professionals on the use of this medicine is stated at the end of this leaflet.

Elderly patients
In elderly patients (up to 75 years of age) without clinically detected liver or kidney insufficiency, dosage adjustment is not usually necessary.
In elderly patients (over 75 years of age) 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. If in your case the insufficiency is mild or moderate, your doctor may recommend prolonging the dosage interval.

Use in children and adolescents
Children aged 1 to 12 years
Usually the single dose of tramadol is 1-2 mg/kg of body weight. The lowest effective analgesic dose usually should be chosen. The daily dose should not exceed the lowest of the following doses – 8 mg/kg of body weight or 400 mg of active substance.
Further information for healthcare professionals on the use of this medicine in children is stated at the end of this leaflet.

The following information is intended for healthcare professionals only.

Please read this information carefully before using Tramadol 50mg/ml Solution for Injection or Infusion. Further information is contained in the Summary of Product Characteristics.

Presentation
Tramadol 50 mg/ml solution for injection/infusion is presented as a clear colourless solution free from visible particles in a colourless borosilicate glass ampoule. Each ampoule contains 2ml of solution (100 mg of tramadol hydrochloride).

Instructions for Tramadol ampoule handling
Tramadol is filled in break-seal ampoules. There is a break line or open point cut on the ampoule, and it is easy to open:
1) turn the ampoule with the breaking site up;
2) break the ampoule downward.

Posology
The dose should be adjusted to the intensity of the pain and the sensitivity of the individual patient. The lowest effective dose for analgesia should generally be selected. The total daily dose of 400 mg tramadol should not be exceeded, except in special clinical circumstances (for example, in case of cancer pain or postoperative severe pain).

Unless otherwise prescribed, Tramadol should be administered as follows:

Adults and adolescents above the age of 12 years
Depending on the intensity of pain, 50–100 mg of tramadol (corresponds to 1-2 ml of Tramadol) is administered every 4–6 hours. The total daily dose of 400 mg (4 ampoules) should not be exceeded.

Elderly patients
A dose adjustment is not usually necessary in patients up to 75 years without clinically manifest hepatic or renal insufficiency. In patients over 75 years elimination may be prolonged. Therefore, if necessary the dosage interval is to be extended according to individual requirements.

Renal insufficiency/dialysis and hepatic insufficiency
In patients with renal and/or hepatic insufficiency the elimination of tramadol is delayed. In these patients prolongation of the dosage intervals should be carefully considered according to the patient's requirements.

Paediatric population
Tramadol should not be used in children under 1 year of age.

For children up to the age of 12, the single dose of tramadol is 1-2 mg per kg body weight. The lowest effective dose for analgesia should generally be selected. The total daily dose must not exceed the lowest of these doses – 8 mg/kg body weight or 400 mg of the active substance.

Method of administration
Intravenous (solution should be administered slowly (1 ml (50 mg of tramadol hydrochloride) per minute), intramuscular or subcutaneous injection.
Tramadol may be diluted with an appropriate solution for infusion (e.g. 0.9 % sodium chloride or 5 % glucose solution) to be administered by intravenous infusion.

For instructions on dilution of the medicinal product before administration, see 'Special precautions for disposal and other handling.'

Duration of administration
Tramadol should under no circumstances be administered for longer than absolutely necessary. If long-term pain treatment with tramadol is necessary in view of the nature and severity of the illness, then careful and regular monitoring should be carried out (if necessary with breaks in treatment) to establish whether and to what extent further treatment is necessary.

Method and duration of administration
Tramadol is slowly injected (1 ml per minute), typically into a blood vessel inside the arm, into the muscle (usually the buttocks) or under the skin. Tramadol can also be diluted and administered by intravenous infusion.
Further information for healthcare professionals on the use of this medicine is stated at the end of this leaflet.

You should not take Tramadol longer than necessary. If long-term treatment is necessary for you, your doctor will carry out regular monitoring (if necessary with breaks in treatment) to establish whether and to what extent further treatment is necessary.

If you think that the effect of Tramadol is too strong or too weak, talk to your doctor or pharmacist.

If you use more Tramadol than you should
If you receive additional dose by mistake, this normally will not have a negative impact. You should take your next dose as prescribed.
After a very large dose, narrowed pupils, vomiting, drop in blood pressure, increased heart rate, acute circulatory weakness or collapse, consciousness disorders up to coma, fits and breathing depression or breathing arrest may occur. In such cases, you should contact your doctor immediately!

If you forget to use Tramadol
If you have not received intended Tramadol injection or infusion, it is expected that the pain will return. Do not take a double dose to make up for a forgotten dose, just continue to take Tramadol as before.

If you stop using Tramadol
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 the treatment with Tramadol is interrupted or completed too quickly, it is expected that the pain will return. If you wish to stop treatment because of adverse effects, please tell your doctor or nurse.
Usually after Tramadol discontinuation no drug withdrawal reactions occur. However in rare cases, patients treated with Tramadol some time may feel unwell if the treatment is stopped abruptly. In these patients agitation, anxiety, nervousness and tremor may occur. Confusion, hyperactivity, sleep disorders, stomach or intestinal problems are possible. Some patients may experience panic attacks, strongly expressed anxiety, hallucinations, abnormal sensations: itching, tingling, numbness and tinnitus. Other unusual CNS symptoms such as confusion, delusion, personality disorders (depersonalization) and changes in a sense of reality (derealization) and the feeling that haunts you (paranoia) very rarely observed.
If after completion of treatment you experience any of these symptoms, please tell your doctor or nurse. If you have any questions about 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.

Usually the frequency of side effects is classified as follows:
Very common (may affect more than 1 in 10 patients):
- dizziness;
- nausea.

Common (may affect less than 1 in 10 patients):
- headache, somnolence;
- constipation, dry mouth, vomiting;
- sweating (hyperhidrosis);
- exhaustion.

Uncommon (may affect less than 1 in 100 patients):
- the effect on heart rate and blood flow (palpitations, increased heart rate, weakness, faint or acute circulatory weakness or collapse). These adverse effects mainly occur during intravenous administration and in patients who are physically stressed;
- retching, upset stomach (e.g. feeling of pressure in the stomach, bloating), diarrhoea;
- skin reactions (e.g. itching, rash, hives).

Rare (may affect less than 1 in 1000 patients):
- allergic reactions (e.g. difficulty breathing, brochospasm, wheezing, skin oedema) and shock (sudden circulatory failure);
- low heart rate;
- high blood pressure;
- abnormal sensations (e.g. itching, tingling, numbness), trembling, epileptic fits, muscle twitches, uncoordinated movements, transient loss of consciousness (syncope), speech disorders; Epileptic fits have occurred mainly after treatment with high doses of tramadol or when tramadol was used concurrently with other medicines that can cause seizures;
- changes in appetite;
- hallucinations, confusion, sleep disorders, delirium, anxiety and nightmares;
- after the treatment with Tramadol psychic complaints may occur. Their intensity and nature may vary (depending on the patient's personality and duration of treatment). They may include mood changes (mainly, elated mood, sometimes irritability), changes in activity (usually suppression, occasionally increased activity), and decreased cognitive and sensory perception (sensory recognition and the changes that can lead to erroneous judgments). Dependence may occur. If the treatment is stopped suddenly, possible drug withdrawal symptoms may occur (see *If you stop using Tramadol*);
- narrowing of the pupils (miosis), excessive enlargement of the pupils (mydriasis), blurred vision;
- slowed breathing, shortness of breath (dyspnoea);
- asthma exacerbations are reported, although it is unknown whether it is caused by tramadol. The recommended dose exceeding or co-administered medicines that suppress brain activity may slow down breathing;
- muscle weakness;
- micturition disorders (urinary retention and less urine excretion than it would normally be (dysuria).

Very rare (may affect less than 1 in 10 000 patients):
- increase in liver enzymes.

Not known (cannot be estimated from the available data):
- low blood sugar.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system: Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

5. How to store Tramadol

Do not refrigerate or freeze.

Keep out of the sight and reach of children.

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

Once ampoule has been opened, the product should be used immediately.

Chemical and physical in-use stability has been demonstrated for 48 hours at 25 °C with 0.9% sodium chloride and 5% glucose solution.
From a microbiological point of view, unless the method of opening/dilution precludes the risk of microbial contamination, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user.

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 contains
– The active substance is tramadol hydrochloride.
1 ml of solution contains 50 mg of tramadol hydrochloride.
One ampoule (1 ml) contains 50 mg of tramadol hydrochloride.
One ampoule (2 ml) contains 100 mg of tramadol hydrochloride.

The other ingredients are sodium acetate trihydrate, water for injections.

What Tramadol looks like and contents of the pack
Clear, colourless solution, free from visible particles.

1 ml or 2 ml of solution in type I hydrolytic class colourless borosilicate glass ampoule with break line or open point cut.
5 ampoules in a PVC liner. 1 liner (5 ampoules) or 2 liners (10 ampoules) in a cardboard box. 20 liners (100 ampoules) in a cardboard box (for hospital use).

Not all pack sizes may be marketed.

Marketing Authorisation HolderAS KALCEKS
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Manufacturer
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This medicinal product is authorised in the Member States of the EEA under the following names:

Latvia:	Tramadol 50 mg/ml šķīdums injekcijām/infūzijām
Lithuania:	Tramadol 50 mg/ml injekcinis ar infuzinis tirpalas
Austria:	Tramadol 50 mg/ml Injektions-/Infusionslösung
Hungary:	Tramadol 50 mg/ml oldatos injekció/infúzió
Czech Republic:	Tramadol
Poland:	Tramadol
United Kingdom:	Tramadol 50 mg/ml solution for injection/infusion
Romania:	Tramadol 50 mg/ml soluție injectabilă/perfuzabilă

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Place for AS Kalceks internal code
Place for manufacturer internal code

Special precautions for disposal and other handling
For single use only.
Tramadol is compatible with 0.9% sodium chloride or 5% glucose solution for infusion.

Calculation of injection volume
1) Calculate the total required dose of tramadol hydrochloride (mg): body weight (kg) x dose (mg/kg).
2) Calculate the injected volume of diluted solution (ml): divide the total dose (mg) by the desired reconstituted concentration (mg/ml; see table below).

Table. Dilution of the Tramadol solution for injection/infusion

Concentration of the diluted solution (tramadol hydrochloride mg/ml)	Tramadol 50 mg/ml solution for injection/ infusion (1 ml ampoule) + added solvent	Tramadol 50 mg/ml solution for injection/ infusion (2 ml ampoule) + added solvent
25.0 mg/ml	1 ml + 1 ml	2 ml + 2 ml
16.7 mg/ml	1 ml + 2 ml	2 ml + 4 ml
12.5 mg/ml	1 ml + 3 ml	2 ml + 6 ml
10.0 mg/ml	1 ml + 4 ml	2 ml + 8 ml
8.3 mg/ml	1 ml + 5 ml	2 ml + 10 ml
7.1 mg/ml	1 ml + 6 ml	2 ml + 12 ml
6.3 mg/ml	1 ml + 7 ml	2 ml + 14 ml
5.6 mg/ml	1 ml + 8 ml	2 ml + 16 ml
5.0 mg/ml	1 ml + 9 ml	2 ml + 18 ml

According to your calculations dilute the content of Tramadol ampoule by adding an appropriate solvent, mix and use the calculated volume of diluted solution.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Excipients
Sodium acetate trihydrate and Water for injections.

Tramadol incompatibilities
Tramadol 50 mg/ml solution for injection/infusion should not be mixed with solution for injection or infusion containing diclofenac, indometacin, phenylbutazone, diazepam, midazolam, flunitrazepam and glyceryl trinitrate.
This medicinal product must not be mixed with other medicinal products except those mentioned under 'Special precautions for disposal and other handling.'

Shelf-life
4 years.

Once ampoule has been opened, the product should be used immediately.

Chemical and physical in-use stability has been demonstrated for 48 hours at 25 °C with 0.9% sodium chloride and 5% glucose solution.
From a microbiological point of view, unless the method of opening/dilution precludes the risk of microbial contamination, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user.

Special precautions for storage
Do not refrigerate or freeze.
For storage conditions after dilution or first opening of the medicinal product, see the 'Shelf-life' section.

Nature and contents of container
1 ml or 2 ml of solution in type I hydrolytic class colourless borosilicate glass ampoule with break line or open point cut.
5 ampoules in a PVC liner. 1 liner (5 ampoules) or 2 liners (10 ampoules) in a cardboard box.
20 liners (100 ampoules) in a cardboard box (for hospital use).