

CTD MODULE 1
ADMINISTRATIVE INFORMATION AND
PRODUCT INFORMATION

Product Name :	TRAMAREN CAPSULES (Tramadol Hydrochloride 50mg)
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Pack Insert

TRAMAREN CAPSULES

Composition: Each capsule contains
Tramadol Hydrochloride BP 50 mg

Therapeutic Indications:

Tramadol is used in the treatment of moderate to severe pain.

PHARMACOLOGICAL PROPERTIES:

Pharmacodynamic Properties:

Tramadol is an analgesic compound (pain killer) belonging to the class of opioids which acts on the central nervous system. It relieves pain predominantly due to blockade of serotonin reuptake and its agonist activity on mu receptor (special nerve cells in the brain and spinal cord).

Compared to morphine, tramadol does not show respiratory depression when given within the analgesic dosage interval and does not affect gastrointestinal motility/movement.

Pharmacokinetic properties:

Absorption

After administration of a single dose of 50mg to 100mg, bioavailability is between 70 and 90%. Oral administration of tramadol with food does not significantly affect its rate and extent of absorption. Peak plasma concentration after oral administration of 100mg tramadol is approximately 300ng/ml (C_{max}) and is reached after about 2 hours.

Distribution

Tramadol crosses the placental barrier and is found in very small amounts in breast milk (about 0.1% of the dose administered to the mother).

Metabolism

Tramadol is extensively metabolized after oral administration and is excreted in urine

Elimination

Tramadol is metabolized predominantly by the liver with a half-life between 5 and 7 hours in healthy volunteers; In the case of renal impairment (Kidney dysfunction) and hepatic impairment (liver disease), tramadol stays longer in the plasma (half-life: 12 hours).

CLINICAL PARTICULARS

Posology and method of administration:

Always take use this medicine exactly as your doctor or pharmacist has told you. The usual doses are given below. Your doctor may gradually increase or decrease your dose depending on how you respond to the treatment. The dosage should be adjusted to the intensity of the pain and patient individual pain sensitivity. In general the lowest pain-relieving dose should be taken.

The capsules are taken by mouth, should be swallowed whole with a glass of water. The capsules can be taken with or without food and should not be chewed.

Adults and children over 12 years

Acute pain: Adults and children over age 12 years: 50-100mg 3-4 times daily. Patients with low weight should use 0.7mg/kg bodyweight. Duration of therapy: as prescribed by physician

Chronic pain: An initial dose of 50mg or 100mg is followed by doses of 50mg or 100mg, every 4 to 6 hours, according to pain severity. The need for continued treatment should be assessed at regular intervals (as withdrawal symptoms and dependence have been reported) by doctor.

A total daily dose of 400mg (8 Capsules) should not be exceeded.

Children below 12 years old

Tramadol is not recommended for use in children below age 12.

Elderly patients: In elderly patients (above 75 years) the excretion of tramadol may be delayed. The normal adult doses may be given but the dosage interval should be extended to 9 hours.

Renal impairment/renal dialysis: The usual initial dosage should be used. For patients with creatinine clearance <30ml/min, the dosage interval should be increased to 12 hours. Tramadol is not recommended in patients with severe renal impairment (creatinine clearance <10ml/min).

Patients with hepatic impairment: The usual dosage should be divided in 2, or the dosage interval should be extended to 12 hours. In severe hepatic impairment, the product should not be taken.

Contraindications:

This product should not be taken in the following situations:

- Previously demonstrated allergy to tramadol or any of the other ingredients in the capsule.
- If you are under the influence of alcohol or sedative drugs including sleeping pills, other pain-killers or tranquiliser medicines
- If you are taking, or have taken in the last two weeks, certain medicines called "monoamine oxidase inhibitors" or MAOIs (used to treat mental illness e.g. depression and the antibiotic linezolid). The combination could result in a serious, potentially life threatening interaction
- Severe liver, kidney or lung (breathing) problem.
- Severely impaired kidney function (creatinine clearance less than 10ml/min).
- Severe respiratory impairment.
- If you have epilepsy (fits) that is not controlled with your current medicine
- Tramadol must not be administered during breastfeeding if long term treatment, i.e more than 2 to 3 days, is necessary (see: *Pregnancy and lactation*).
- Are pregnant, planning to become pregnant or breastfeeding.
- Are undergoing treatment to withdraw from use of narcotics

Special warnings and precautions for use.

Talk to your doctor or pharmacist before taking Tramadol

- If you suffer from epilepsy or seizures (fits) or have had them in the past because tramadol could increase the risk of you having further fits
- If you have liver or kidney problems.
- As with all painkillers of this type (opioid analgesics), tramadol should be used with caution, and only under medical supervision in seriously ill patients including those with breathing difficulties, excessively low blood pressure (shock due to severe injury or blood loss), decreased consciousness, serious head injury or brain diseases that may cause elevated pressure in the skull.
- As with all medicines of this type, tramadol may lead to psychological and physical dependence or addiction in some people, especially with long term use. The dose needed to achieve the desired effect may increase with time. Tramadol should be used with caution, and only for short periods, in patients who are addicted to other opioid pain-killers.
- 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.

Interactions with other medicinal products and other forms of interactions

The risk of side effects increases.

- If you are taking medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk of having a fit may increase if you take Tramadol capsules at the same time. Your doctor will tell you whether Tramadol capsules are suitable for you.

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•If you are taking certain antidepressants. Tramadol capsules 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.

•The pain-relieving effect of Tramadol may be weakened and/or shortened if you also take medicines containing: - carbamazepine (used to treat epilepsy) - pentazocine, nalbuphine or buprenorphine (pain killers) - ondansetron (used to stop you feeling sick), Cimetidine (for gastric ulcers).

•Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicine. Especially:

•Monoamine Oxidase Inhibitors (MAOIs, e.g. moclobemide), or have taken these within the last 2 weeks.

•Any opioid medicines which include strong pain killers such as morphine, pethidine, buprenorphine, nalbuphine and pentazocine.

•Medicines which slow your reactions and breathing down. Carbamazepine (for epilepsy or nerve pain).

•Sedative medicines/sleeping tablet such as tranquilizers, sleeping pills, antidepressants and other pain relievers

(morphine, codeine) as you may feel excessively drowsy or feel that you might faint

•Medicines that prevent blood clotting, such as warfarin; the dose of these medicines may need to be reduced,

otherwise there could be an increased risk of potentially serious bleeding.

•Medicines to treat depression (including fluoxetine, paroxetine, amitriptyline or lofepramine) and medicines to treat anxiety or mental illness.

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.

Tramadol capsules with food, drink or alcohol

You are advised NOT to drink alcohol with this medicine. The effects of Tramadol capsules are not affected by food.

Pregnancy and breast-feeding

There is very little information regarding the safety of tramadol during pregnancy therefore do not take Tramadol capsules if you are pregnant. 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.

Chronic use of tramadol may induce - at any dosage- a withdrawal syndrome in newborns. At the end of pregnancy,

high dosages, even for short-term treatment, may induce respiratory depression in the newborn.

Breast-feeding

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

Effects on ability to drive and use machines

Tramadol may cause drowsiness and this effect may be intensified by alcohol and other CNS depressants. If this happens,

do not drive or operate machinery.

If you forget to take Tramadol: If you forget to take Tramadol take it as soon as you remember and then carry on as before. Do not take a double dose to make up for a forgotten dose. **Overdose**

If you have taken more capsules than you have been told to take, contact your doctor immediately or go to your nearest hospital casualty department. A number of symptoms may occur, which might include: vomiting (being sick), a fall in blood pressure, a fast heartbeat, collapse, fainting or even coma, epileptic fits and difficulties in breathing.

Supportive first aid measures such as keeping the airway open and ensuring cardiovascular function should be done; naloxone can be used to reverse respiratory depression; fits can be controlled with diazepam.

If you stop taking Tramadol: If you stop taking Tramadol, your pain may return. If you would like to stop treatment because you have unpleasant side effects, please talk to your doctor. If you have been taking this medicine for a very long time, you may get the following side effects if you suddenly stop treatment: restlessness, anxiety, nervousness, shaking or an upset stomach. If you get any of these effects after stopping treatment with Tramadol please talk to your doctor.

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

Possible side effects:

Tramadol can occasionally cause allergic reactions although serious allergic reactions (including anaphylaxis and angioedema) are rare. Contact a doctor or emergency unit immediately if you experience any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

The same applies in case of seizures ("fits").

The frequency of side effects is classified as follows:

Common: affects 1 to 10 users in 100

Uncommon: affects 1 to 10 users in 1,000

Rare: affects 1 to 10 users in 10,000

Very rare: affects less than 1 user in 10,000

Not known: frequency cannot be estimated from the available data.

The following side effects may occur:

Very common nausea; dizziness.

Common: headache, sleepiness; vomiting (being sick), constipation, dry mouth; sweating.

Uncommon: Irregular, rapid beating or pulsation of the heart, increased heartbeat, low blood pressure (especially when standing upright), this may lead to collapse. Diarrhoea, retching, gastrointestinal irritation (a feeling of pressure in the stomach, bloating); skin disorders (e.g. itchiness, rash, sudden onset of skin redness).

Rare: Slow heartbeat, rise in blood pressure; sleepiness, change in appetite, tingling skin sensation (e.g. pins and needles); trembling, breathing difficulties, epileptic-like seizures ("fits"), uncoordinated movement, muscle twitches, fainting; blurred vision; difficulty in passing urine and urinary retention. Muscle weakness. Generalized allergic reactions (e.g. anaphylaxis and angioedema, see below). Hallucinations, confusion, anxiety, sleep disturbance and nightmares, changes in mood (high or low spirits), changes in activity (slowing down but sometimes an increase in activity) and being less aware and less able to make decisions, which may lead to errors in judgement.

Frequency not known:

Increased levels of liver enzymes.

Worsening of asthma has been reported,

however it has not been established whether

it was caused by tramadol. Speech disorders,

decrease in blood sugar level.

During use of Tramadol, dependence, abuse and addiction may occur. When treatment is stopped, symptoms of withdrawal reactions may occur, such as agitation, anxiety, nervousness, sleeplessness, uncontrolled muscular action (hyperkinesia), tremor and gastrointestinal symptoms. Other symptoms that have very rarely been seen with tramadol discontinuation e.g., panic attacks, severe anxiety, hallucinations, tingling skin sensation, hearing sounds e.g. ringing or buzzing, without an external cause (tinnitus).

Special precautions for storage:

Keep out of the sight and reach of children.

Store at a Temperature not exceeding 25°C.

Do not use Tramadol capsules after the expiry date stated on the label/carton

Presentation:

Blister pack of 10x10 capsules

MANUFACTURED BY:

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 A Milestone To Golden Health