

INSTRUCTIONS FOR USE

Please read the following instructions for use carefully before you start taking this medicine.

- Please keep these instructions. You may want to read them again later.
- If you have any questions, please ask your doctor or pharmacist.
- This medicine has been prescribed only for you and must not be given to anyone else. It may harm other people even if they have the same illness as you.

This package information leaflet tells you:

1. What are TRAMAL® capsules and what are they used for?
2. What must you take into account before using TRAMAL® capsules?
3. How should you take TRAMAL® capsules?
4. Which side-effects may occur?
5. How should you store TRAMAL® capsules?

TRAMAL® capsules, hard capsules

Active substance: tramadol hydrochloride



- The active ingredient of TRAMAL® capsules is tramadol hydrochloride. One TRAMAL® hard capsule contains 50 mg tramadol hydrochloride.
 - The other ingredients are: Microcrystalline cellulose, sodium carboxymethyl starch (type A) (Ph.Eur.), colloidal anhydrous silica, magnesium stearate (Ph.Eur.), gelatin, indigotine, ferric oxides and hydroxides (E 172), titanium dioxide (E 171), sodium lauryl sulphate
- TRAMAL® capsules are supplied in packs of 10, 30, and 50 hard capsules.

1. WHAT ARE TRAMAL® CAPSULES AND WHAT ARE THEY USED FOR?

Tramadol - the active substance in TRAMAL® capsules - 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.

from:

Grünenthal GmbH - 52099 Aachen

Tel. +49 241 569-0

Fax +49 241 569-1498

TRAMAL® capsules are used for the treatment of moderate to severe pain.

2. WHAT MUST YOU TAKE INTO ACCOUNT BEFORE USING TRAMAL® CAPSULES?

TRAMAL® capsules must not be taken,

- if you are allergic to tramadol or any of the other ingredients of TRAMAL® capsules .
- in acute poisoning with alcohol, sleeping pills, pain relievers or other psychotropic medicines (medicines that affect mood and emotions).
- if you are also taking MAO inhibitors (certain medicines used for depression) or have taken them in the last 14 days before treatment with TRAMAL® capsules (see "Interactions with other medicines").
- if you are an epileptic and your fits are not adequately controlled by treatment.
- as a substitute in drug withdrawal.

Particular caution is necessary when taking TRAMAL® capsules,

- 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 it);
- 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;
- if you suffer from a liver or kidney disease.

In such cases please consult your doctor before taking the medicine.

Please note that TRAMAL® capsules may lead to physical and psychological addiction. When TRAMAL® capsules are taken for a long time, their effect may decrease, so that higher doses have to be taken (tolerance development). In patients with a tendency to abuse medicines or who are dependent on medicines, treatment with TRAMAL® capsules should only be carried out for short periods and under strict medical supervision.

Please also inform your doctor if one of these problems occurs during treatment with TRAMAL® capsules or if they applied to you in the past.

Children

TRAMAL® capsules are not intended for use in children below the age of 12 years.

Pregnancy

If you are pregnant, your doctor will prescribe TRAMAL® capsules only if absolutely necessary. In general, use of TRAMAL® capsules under these circumstances is not recommended, as safety has not been investigated in pregnant women. The repeated administration of TRAMAL® capsules during pregnancy may lead to habituation in the unborn child and as a result, the child may experience withdrawal symptoms after birth.

When given before or during birth, TRAMAL® capsules do not affect the ability of the womb to contract, which is important for natural birth.

Before using any medicines please ask your doctor or pharmacist for advice.

Breast-feeding

About 0.1% of the dose taken by the mother passes into the milk. On a single dose it is usually not necessary to interrupt breast-feeding; otherwise please ask your doctor for advice.

Driving and operating machinery

TRAMAL® capsules may influence 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, and do not work without a firm hold!

Important information about certain other ingredients of TRAMAL® capsules

None.

Interactions with other medicines

Please inform your doctor or pharmacist if you are taking or have recently taken other medicines, even if they do not require a prescription.

The pain-relieving action of TRAMAL® capsules may be reduced and the length of time it acts may be shortened,

- if you take medicines which contain carbamazepine (for epileptic fits).
- The risk of side-effects increases,
- if you take medicines which also depress brain function together with TRAMAL® capsules.
- if medicines which provoke fits or reduce the seizure threshold (e.g. medicines for the treatment of certain psychological diseases) are taken at the same time. Epileptic fits have been observed on very rare occasions.
- if you take serotonergic medicines (for the treatment of depression) together with TRAMAL® capsules. In rare cases this may lead to serotonin syndrome. Symptoms of serotonin syndrome are, for example, confusion, restlessness, high temperature, sweating.
- if you take medicines which prevent abnormal blood clotting - called coumarin derivatives (e.g. warfarin) together with TRAMAL® capsules. The action of these medicines on blood clotting may be affected and small areas of bleeding under the skin (ecchymosis) may appear.

Other possible interactions

- TRAMAL® capsules should not be taken together with MAO inhibitors (medicines for the treatment of depression). When MAO inhibitors were taken 14 days before the administration of another opioid (pethidine), life-threatening interactions affecting the central nervous system, breathing and circulation were observed.
- The same interactions with MAO inhibitors cannot be ruled out during treatment with TRAMAL® capsules.

What food and beverages should be avoided?

Do not drink alcohol during treatment with TRAMAL® capsules, as the effects of TRAMAL® capsules and alcohol may intensify each other.

This is a medicament

Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you. Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers

Union of Arab Pharmacists

3. HOW SHOULD YOU TAKE TRAMAL® CAPSULES?

You should take TRAMAL® capsules exactly according to your doctor's instructions. Please ask your doctor or pharmacist if you are not quite sure.

The dosage should be adjusted to the intensity of the pain and the sensitivity of the individual patient. In general the lowest pain-relieving dose should be taken. Unless otherwise prescribed by your doctor, the usual dose is:

Adults and adolescents from the age of 12 years

For moderate pain one TRAMAL® hard capsule (equivalent to 50 mg tramadol hydrochloride). If there is no effect after 30-60 minutes, a second capsule can be taken.

If for severe pain a higher dose is necessary, two TRAMAL® hard capsules (equivalent to 100 mg tramadol hydrochloride) may be taken.

Depending on the intensity of the pain the effect lasts for 4-8 hours. Daily doses of eight TRAMAL® hard capsules (equivalent to 400 mg tramadol hydrochloride) should not be exceeded, unless prescribed by your doctor.

Elderly patients

In acute pain TRAMAL® capsules are taken only once or a small number of times. Therefore it is not necessary to adjust the dose. 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

In acute pain TRAMAL® capsules are taken only once or a small number of times. Therefore it is not necessary to adjust the dose. Patients with severe liver and/or kidney insufficiency should not take TRAMAL® capsules. In less severe cases your doctor may recommend prolonging the dosage interval.

How and when should you take TRAMAL® capsules?

You should not chew TRAMAL® capsules and take them with sufficient liquid. The hard capsules may be taken independent of meals.

How long should you take TRAMAL® capsules?

You should not take TRAMAL® capsules for longer than necessary. If the nature and severity of the disease require long-term treatment with TRAMAL® capsules, a careful check should be made at regular short intervals as to whether and to what extent this is medically necessary (if necessary with breaks in treatment) and if so, in which dosage.

Please consult your doctor if you feel that the effect of TRAMAL® capsules is too strong or too weak.

If you have taken more TRAMAL® capsules than you should:

If you have taken two single doses of TRAMAL® capsules at once by mistake, this will generally have no negative effects. If pain returns, you should continue taking TRAMAL® capsules as usual.

After taking very high doses, pin-point or wide pupils, vomiting, fall in blood pressure, fast heart-beat, feeling faint, reduced level of consciousness up to coma (deep unconsciousness), epileptic fits, and difficulty in breathing up to stoppage of breathing may occur. In such cases call the nearest doctor immediately!

If you have forgotten to take TRAMAL® capsules:

If you forget to take the hard capsules, pain may return. Do not double the dose, simply continue taking the capsules as before.

Effects if treatment with TRAMAL® capsules is stopped:

If you interrupt or stop treatment with TRAMAL® capsules too soon, pain is likely to return. If you wish to stop treatment on account of unpleasant side-effects, please consult your doctor.

In general stopping treatment with TRAMAL® capsules will have no after-effects. In some patients who have taken TRAMAL® capsules over a very long period of time, however, some after-effects such as restlessness, anxiety, panic attacks, hallucinations, unusual perceptions such as itching, tingling and numbness, noise in the ears (tinnitus), nervousness, sleeplessness, trembling or stomach and bowel problems may occur. If one of these side-effects occurs after stopping treatment with TRAMAL® capsules, please consult your doctor.

4. WHICH SIDE-EFFECTS MAY OCCUR?

Like all medicines TRAMAL® capsules may have side-effects. Usually these are classified as follows:

- very common (more frequently than 1 in 10 patients),
 - common (more frequently than 1 in 100 patients),
 - uncommon (more frequently than 1 in 1,000 patients),
 - rare (more frequently than 1 in 10,000 patients),
 - very rare (1 or less than 1 in 10,000 patients, including isolated cases).
- The most common side-effects during treatment with TRAMAL® capsules are nausea and dizziness, which occur more frequently than 1 in 10 patients.

Heart and circulation problems

- uncommon (< 1%): effects on the heart and blood circulation (pounding of the heart, fast heart-beat, feeling faint or collapse). These side-effects may appear particularly when the patient is in an upright position or under physical strain.
- slow heart-beat, increase in blood pressure.

- rare (< 0.1%):
- Nervous system complaints
- very common (> 10%): dizziness.
- common (1-10%): headaches, muzziness.
- rare (< 0.1%): changes in appetite, abnormal sensations (e.g. itching, tingling, numbness), trembling, slow breathing, epileptic fits.
- If the recommended doses are exceeded, or if other drugs are taken which depress brain function, slow breathing may occur.
- Epileptic fits occurred frequently after taking high doses of tramadol or when medicines that may cause fits themselves or reduce the fit threshold were taken at the same time.

Psychological side effects

- rare (< 0.1%): hallucinations, confusion, sleep disorders and nightmares.
- Psychological complaints may appear after treatment with TRAMAL® capsules. 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 (changes in senses and recognition, which may lead to errors in judgement).
- Dependence may occur.

Visual disorders

- rare (< 0.1%): blurred vision

Difficulty in breathing

- Worsening of asthma has also been reported, but it has not been established whether it was caused by the active substance tramadol.

Stomach and bowel problems

- very common (> 10%): nausea
- common (1-10%): vomiting, constipation, dry mouth.
- uncommon (< 1%): urge to vomit, stomach trouble (e.g. feeling of pressure in the stomach, bloating)

Skin and skin appendages

- common (1-10%): sweating
- uncommon (< 1%): skin reactions (e.g. itching, rash).

Bones and muscles

- rare (< 0.1%): weak muscles.

Liver and bile complaints

- very rare (< 0.01%): increase in liver enzyme values

Difficulties in passing water

- rare (< 0.1%): difficulties in passing water or less urine than normal.

General condition

- rare (< 0.1%): allergic reactions (e.g. difficulty in breathing, wheezing, swelling) and shock (sudden circulation failure) have occurred in very rare cases.
- If TRAMAL® capsules are taken over a long period of time dependence may occur, although the risk is very low. At the end of medication, signs of withdrawal may appear (see "Effects when treatment with TRAMAL® capsules is stopped").

If you experience one of the above mentioned serious side-effects, call the nearest doctor immediately. If you experience side-effects that are not listed in this package insert, please inform your doctor or pharmacist.

5. HOW SHOULD YOU STORE TRAMAL® CAPSULES?

Do not store above 30°C. The expiry date of this pack is printed on the top of the folding box and on the edge of the capsule strip. Do not use TRAMAL® capsules after this date.

Keep medicines out of children's reach.

Date of information

June 2004