Patient package insert according to Pharmacists' Regulations (Preparations)-1986
This medicine can be sold with a physician's prescription only

Tramaraz 100 mg/ml
Drops for oral use

Each 1 ml (40 drops) contains:
Tramadol Hydrochloride 100 mg.

Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine".

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is the same as yours.

This medicine is not intended for children under the age of 14 years.

Opioid medicines can cause addiction (mainly with prolonged use), and potential abuse and overdose are possible. The reaction to overdose can be slow breathing and even death.
Make sure that you know the name of the medicine, the dosage you are taking, how often you take it, the duration of treatment, its side effects and potential risks.

Additional information about the risk of dependence and addiction can be found at:
https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

Taking this medicine with benzodiazepines, other central nervous system depressants (including street drugs) or alcohol can cause severe drowsiness, breathing problems (respiratory depression), coma and death.

1. What is the medicine intended for?
Tramaraz 100 mg/ml is intended for the treatment of moderate to severe pain.

Therapeutic group: opioids.

Tramadol, the active substance in **Tramaraz 100 mg/ml**, is a painkiller belonging to the class of medicines called opioids and it acts on the central nervous system. It relieves pain by acting on specific nerve cells of the spinal cord and brain.

2. Before using the medicine:
Do not use the medicine:

- If you are sensitive (allergic) to the active ingredient (Tramadol Hydrochloride) or to any of the other ingredients this medicine contains (see section 6).
- If you are in a state of acute poisoning with alcohol, sleeping pills, pain relievers or other psychotropic medicines (medicines that affect mood and emotions).
- If you are taking monoamine oxidase inhibitors (MAO) (certain medicines for the treatment of depression), or if you have taken them in the last 14 days before taking **Tramaraz 100 mg/ml** (see section "Drug interactions").
- If you are an epileptic and your fits are not adequately controlled by the treatment you receive.
- As a substitute in drug withdrawal.

Special warnings regarding the use of the medicine

Before the treatment with Tramaraz 100 mg/ml, tell the doctor if:
- You think that you are or have ever been dependent on other pain relievers (opioids), alcohol, prescription medicines, or any illegal drug.
- You have previously suffered from withdrawal symptoms such as: agitation, anxiety, shaking or sweating when you have stopped using alcohol or drugs.
- You feel a need to take more **Tramaraz 100 mg/ml** to get the same level of pain relief, this may indicate the beginning of tolerance to the effects of the medicine and the beginning of addiction to it. Contact your doctor who will discuss your treatment and may change your dosage or switch the treatment to another pain reliever.
- You suffer from consciousness disorders (if you feel that you are going to faint).
- You are in a state of shock (cold sweat can be a sign of this).
- You suffer from increased pressure on the brain (can occur after a head injury or brain disease).
- You have difficulty in breathing.
- You have epilepsy or a tendency towards fits, as the risk of fits may increase.
- You suffer from depression and you are taking antidepressants as some of them may interact with tramadol (see below "Drug interactions").
- You suffer from a liver or kidney disease.

Sleep-related breathing problems

Tramaraz 100 mg/ml contains an active ingredient that belongs to a group of medicines called opioids. Opioids can cause sleep-related breathing problems, for example pauses in breathing during sleep (shallow breathing/sleep apnea) and sleep-related hypoxemia (low level of oxygen in the blood). The risk of experiencing pauses in breathing during sleep is dependent on the dosage of the opioid. Your doctor may consider decreasing the total opioid dosage you are taking if you experience pauses in breathing during sleep.

There is a small risk of experiencing serotonin syndrome that may occur after taking tramadol in combination with certain antidepressants or after taking tramadol alone. Seek medical advice immediately if you have any of the symptoms related to this serious syndrome (see section 4 "side effects").

Epileptic fits have been reported in patients taking tramadol at the recommended dosage level. The risk may be increased when dosages of tramadol exceed the upper limit of the recommended daily dose (400 mg).
Taking this medicine regularly, particularly for a long time, can lead to addiction. Your doctor should have explained how long you will be taking it for, when it is appropriate to stop and how to do this safely.
Rarely, increasing the dosage of this medicine may make you more sensitive to pain. If you experience this, speak to your doctor about the treatment.
Addiction can cause withdrawal symptoms when you stop taking this medicine. Withdrawal symptoms can include restlessness, difficulty sleeping, irritability, agitation, anxiety, palpitations, increased blood pressure, nausea or vomiting, diarrhea, loss of appetite, shaking or sweating. Your doctor will discuss with you how to gradually reduce your dose before stopping the medicine. It is important that you do not stop taking the medicine suddenly as you will be more likely to experience withdrawal symptoms.

Opioids should only be used by those the doctor prescribed them for. Do not give your medicine to anyone else. Taking a higher dose or more frequent doses of opioids may increase the risk of addiction. Overuse and misuse can lead to overdose and/or death.

Tramadol is transformed in the liver by an enzyme. Some people have a certain variation of this enzyme and this can affect them in different ways. In some people, they may not get enough pain relief but other people may have serious side effects and more frequently. If you notice any of the following side effects, you must stop taking the medicine and contact your doctor immediately: slow or shallow breathing, confusion, sleepiness, small pupils, nausea or vomiting, constipation, lack of appetite.

Talk to your doctor if you experience any of the following symptoms while taking **Tramaraz 100 mg/ml:**
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.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Tramaraz 100 mg/ml should not be taken together with MAO inhibitors (certain medicines for the treatment of depression), or if you have taken them during the 14 days before taking **Tramaraz 100 mg/ml.**

The pain-relieving effect of **Tramaraz 100 mg/ml** may be reduced and the length of time it acts may be shortened, if you take it with medicines that contain:
- Carbamazepine (for the treatment of epileptic fits)
- Ondansetron (to prevent nausea)

Your doctor will tell you if you need to take **Tramaraz 100 mg/ml,** and which dose.
The risk of side effects may increase if you take:
- Other painkillers such as morphine and codeine (also to ease coughing) or alcohol while you are taking **Tramaraz 100 mg/ml**. You may feel drowsy or that you might faint. if this happens to you, refer to your doctor.
- Concomitant use of **Tramaraz 100 mg/ml** and tranquillizers or sleeping pills (e.g. benzodiazepines), increases the risk of drowsiness, breathing difficulties (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other medicinal options are not possible. However, if your doctor prescribes **Tramaraz 100 mg/ml** together with sedating medicines the dosage and duration of concomitant treatment should be limited by the doctor. Please tell your doctor about all sedating medicines you are taking, and carefully follow your doctor's dosage recommendations. Asking friends or relatives to be aware of the signs and symptoms can help. Contact your doctor if you experience these symptoms.
- Medicines which may cause convulsions (epileptic fits), such as certain types of anti-depressants or anti-psychotics. The risk of having a fit may increase if you take **Tramaraz 100 mg/ml** at the same time. Your doctor will tell you whether **Tramaraz 100 mg/ml** is suitable for you.
- Certain anti-depressants. **Tramaraz 100 mg/ml** may interact with them and you may experience serotonin syndrome (see section 4 "side effects").
- Coumarin anticoagulants (medicines for blood thinning), like warfarin. The effect of these medicines on blood clotting may be affected and bleeding may occur.

Use of the medicine and food
Food does not influence the effect of **Tramaraz 100 mg/ml**.

Use of the medicine and alcohol consumption
Do not drink alcoholic beverages during treatment with **Tramaraz 100 mg/ml**, as its effect may be intensified.

Children and adolescents
Use of **Tramaraz 100 mg/ml** 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.

Pregnancy, breastfeeding and fertility
Do not take **Tramaraz 100 mg/ml** if you are pregnant, or think you might be pregnant unless you have discussed this with your doctor and the benefits of treatment outweigh the risk of harm to the baby. If you take **Tramaraz 100 mg/ml** during pregnancy, it may cause your baby to become dependent and experience withdrawal symptoms after the birth, which require treatment. Do not take **Tramaraz 100 mg/ml** while breastfeeding because tramadol passes into breast milk and may affect your baby. Based on human experience, tramadol does not influence female or male fertility.

Driving and using machines
Tramaraz 100 mg/ml may cause drowsiness, dizziness and blurred vision, and therefore may impair your reactions. If you feel that your reactions are affected, do not drive a car or other vehicle, do not operate electric tools or machinery. The medicine can affect your ability to drive as it may make you sleepy or dizzy. Do not drive while taking this medicine until you know how it affects you. Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine. As for children, they should be warned about riding a bicycle or playing near roads etc.

Important information about some of the ingredients of the medicine
This medicine contains sucrose. Each ml contains 100 mg sucrose.
If you have been told by a doctor that you have an intolerance to some sugars, consult the doctor before taking this medicine. it may damage the teeth.
This medicine contains macrogolglycerol hydroxystearate, which may cause stomach discomfort and diarrhea.
This medicine contains 250 mg of propylene glycol per ml (40 drops).
This medicine contains less than 1 mmol sodium (23mg) per ml (40 drops), that is to say essentially "sodium-free".

3. How to use the medicine?
Always use this medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine. The dosage and manner of treatment will be determined by the doctor only.
The dosage should be adjusted to the intensity of the pain and your individual sensitivity to pain. In general, the lowest pain-relieving dose should be taken.
Do not take more than 400mg tramadol hydrochloride (160 drops) daily, unless your doctor has instructed you to do so.

Unless otherwise instructed by your doctor, the usual recommended dose is:
Adults and adolescents 14 years of age and older
50-100 mg tramadol hydrochloride (20-40 drops) every 4-6 hours.

Children
Tramaraz 100 mg/ml is not intended for children under 14 years of age.

Elderly population
In the elderly population (over 75 years of age), the excretion of tramadol from the body may be delayed. If this applies to you, your doctor may recommend increasing the dosage intervals.

Severe liver or kidney disease (failure)/dialysis patients
Patients with severe liver and/or kidney failure should avoid taking **Tramaraz 100 mg/ml**. If you have mild or moderate failure, your doctor may recommend increasing the dosage interval.

Do not exceed the recommended dose.

Manner of administration
- Swallow with a little water or dribble on some sugar.
- **Pay Attention!** Be sure to measure the dose in the dropper of the bottle.
- The bottle has a safety closure that prevents children from opening it.
- To open: Click on the lid and turn it. To remove the drops, hold the bottle upside down (with the lid down) vertically. After the use screw the lid to close completely.

How long should you take Tramaraz 100 mg/ml?
Your doctor should have discussed with you how long the course of treatment will last and arranged a plan for stopping treatment. This plan outlines how to gradually reduce the dosage until you stop taking the medicine.

If you have accidentally taken a higher dosage
Usually, if you have taken an additional dose by mistake, there should be no negative effects. Continue to take the next dose as prescribed.
If you (or someone else) swallow a lot of **Tramaraz 100 mg/ml** at once, go immediately to the hospital or doctor. Bring the medicine package with you.
Signs of an overdose include very small pupils, vomiting, a fall in blood pressure, fast heart beats, collapse, loss of consciousness, fits and breathing difficulties or shallow breathing.

If you forgot to take the medicine
If you forgot to take **Tramaraz 100 mg/ml**, pain is likely to return. Do not take a double dose to make up for a forgotten dose, simply continue taking the medicine as before.

If you stop taking the medicine
Do not suddenly stop taking this medicine. If you want to stop taking the medicine, consult the doctor first. He will explain to you how to do this, usually by gradually reducing the dosage, such that any unpleasant withdrawal effects will be minimal.
Withdrawal symptoms such as restlessness, sleeping difficulties, irritability, agitation, anxiety, palpitations, increased blood pressure, nausea or vomiting, diarrhea, shaking or sweating may occur if you suddenly stop taking this medicine. Continue with the treatment as recommended by the doctor. Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

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

4. Side effects
Like any medicine, the use of **Tramaraz 100 mg/ml** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.
You should see a doctor immediately if you experience symptoms of an allergic reaction such as swollen face, tongue and/or throat, and/or difficulty swallowing or hives (red bruises on the skin) together with breathing difficulties.

Very common side effects (effects that occur in more than 1 in 10 users):
- Dizziness
- Nausea

Common side effects (effects that occur in 1-10 out of 100 users):
- Headache, drowsiness.
- Fatigue.
- Constipation, dry mouth, vomiting.
- Sweating.

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):
- Effects on the heart and blood circulation (palpitations, fast heartbeat, feeling faint or collapse). These adverse effects may particularly occur in patients in an upright position or under physical strain.
- Urge to vomit, stomach trouble (such as a feeling of pressure in the stomach, bloating), diarrhea.
- Skin reactions (e.g. itching, rash).

Rare side effects (effects that occur in 1-10 out of 10,000 users):
- Allergic reactions (e.g. breathing difficulties, wheezing, swelling of skin) and shock (sudden blood circulation failure).
- Slow heartbeat.
- Increase in blood pressure.
- Abnormal sensations (e.g. itching, tingling, numbness), trembling, epileptic fits, muscle twitches, uncoordinated movement, temporary loss of consciousness (fainting), speech disorders.
- Epileptic fits have occurred mainly at high dosages of tramadol or when tramadol was taken together with other medicines which may induce fits.
- Changes in appetite.
- Hallucination, confusion, sleep disorders, delirium, anxiety and nightmares.
- Complaints about psychological problems may appear after treatment with **Tramaraz 100 mg/ml**. Their intensity and nature may vary (according to the patient's personality and the duration of the treatment). These may appear as a change in mood (mostly high spirits, occasionally irritated), changes in activity (usually a decline, occasionally an increase) and decreased cognitive and sensory perception (decreased awareness and decreased ability to make decisions, which may lead to errors in judgement).
- Blurred vision, excessive dilation of the pupils, constriction of the pupils.
- Slow breathing, shortness of breath.
- Worsening of asthma has been reported, however it has not been proven it was caused by tramadol. If the recommended doses are exceeded, or if other medicines that depress brain function are taken at the same time, breathing may slow down.
- Weak muscles.
- Passing urine with difficulty or pain, passing less urine than normal.

Very rare side effects (effects that occur in less than 1 in 10,000 users):
- Increased liver enzymes.

Side effects with unknown frequency (effects for which a frequency has not yet been determined):
- Low blood sugar level.
- Hiccups.
- Serotonin syndrome, that can manifest as mental status changes (including symptoms such as: 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 "Before using the medicine").
- Dependence and addiction (see below "How do I know if I am addicted").

Drug withdrawal:
When you stop taking **Tramaraz 100 mg/ml**, withdrawal symptoms may be experienced, including restlessness, sleeping difficulties, irritability, anxiety, palpitations, increased blood pressure, nausea, diarrhea, shaking, sweating.

How do I know if I am addicted?
If you notice any of the following signs while taking **Tramaraz 100 mg/ml**, this could be a sign of addiction:
- You feel a need to take the medicine for longer than advised.
- You feel you need to use more than the recommended dosage.
- You are using the medicine for reasons other than prescribed.
- When you stop taking the medicine you feel unwell, and you feel better once taking the medicine again.

If you notice any of these signs, it is important that you talk to your doctor.

If a side effect appears, if one of the side effects worsens or if you suffer from a side effect which is not mentioned in this leaflet, consult the doctor.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking the link "Report side effects due to medicinal treatment" that can be found on the homepage of the Ministry of Health website (www.health.gov.il) directing to an online form for reporting side effects, or by clicking the link: https://sideeffects.health.gov.il.

5. How to store the medicine?
- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. Date) stated on the package. The expiry date refers to the last day of that month.
- **Storage condition:**
  - Store below 25°C.
  - Do not use this medicine for more than 21 months from the day it was opened.
  - Store in the original package.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information
In addition to the active ingredient, the medicine also contains:
Glycerol, propylene glycol, sucrose, macrogolglycerol hydroxystearate, peppermint aroma, sodium cyclamate, potassium sorbate, saccharin sodium, anise aroma, purified water.

What the medicine looks like and what the package contains:
Transparent to light yellow solution, slightly viscous.
The medicine bottle includes a dropper for accurate measurement of the amount of medicine. Each bottle contains 10 ml of the product.

Registration holder:
RAZ Pharmaceuticals Ltd., 31 Gesher Haetz St., Industrial Park, Emek Hefer, Israel.

Manufacturer:
ABC Farmaceutici S.p.A., Italy

Drug registration number at the national drug registry of the Ministry of Health:154-88-34205-00

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