



## **Patient package insert according to Pharmacists' Regulations (Preparations) – 1986**

This medicine can be sold with a physician's prescription only

### **TRAMADEX® OD 100, 200, 300 Prolonged release tablets**

Each prolonged release tablet contains Tramadol hydrochloride 100, 200 or 300 mg, respectively.

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 the medicine.** This leaflet contains concise information about the medicine. If you have any further questions, refer to 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 similar to yours.

**Opioid medicines can cause addiction, especially with prolonged use, and they have a potential for abuse and overdose. A reaction to overdose can manifest as slow breathing and even cause death.**

**Make sure you know the name of the medicine, the dosage you are taking, how often you take it, the duration of treatment, side effects and the 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](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?**

For the treatment of moderate to severe pain.

**Therapeutic group:** opioid pain reliever.

#### **2. Before using the medicine**

##### **Do not use the medicine:**

- If you are hypersensitive (allergic) to the active ingredient (tramadol hydrochloride), or to any of the other ingredients this medicine contains (see section 6).
- In acute poisoning with alcohol, sleeping pills, pain relievers or other psychotropic medicines (medicines that affect mood and emotions).
- If you are taking or have taken in the last two weeks medicines from the monoamine oxidase inhibitors (MAOIs) group (certain medicines to treat depression).
- If you are suffering from severe liver disease or severe kidney disease.
- If you are suffering from epilepsy, not adequately controlled by treatment.
- As a substitute in drug withdrawal.
- If you are breastfeeding, in the case of long-term treatment (see also section "Pregnancy, breastfeeding and fertility").

**If you are not sure, it is important to consult the doctor or pharmacist.**

#### **Special warnings regarding the use of the medicine**

Consult the doctor or pharmacist before the treatment with **Tramadex OD**.

If you feel you need to take more of **Tramadex OD** to get the same level of pain relief, this may mean you are becoming tolerant to the effects of this medicine or are

becoming addicted to it. Speak to your doctor who will discuss your treatment and may change your dose or switch you to an alternative pain reliever.

Tell the doctor if you are addicted to another drug, are being treated for withdrawal from another drug or are dependent on another drug. In patients with a tendency to become addicted to drugs, this medicine should only be used for very short periods and under strict medical supervision.

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 and when it is appropriate to stop and how to do this safely.

Rarely, increasing the dose of this medicine can make you more sensitive to pain. If this happens, you need to speak to your doctor about your treatment.

Addiction can cause withdrawal symptoms when you stop taking this medicine. Withdrawal symptoms can include restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhea, loss of appetite, shaking, shivering 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 they are prescribed for. Do not give your medicine to anyone else. Taking higher doses 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 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 are more likely to get serious side effects. If you notice any of the following side effects, stop using the medicine and seek immediate medical advice: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation, lack of appetite.

#### Sleep-related breathing disorders

**Tramadex OD** can cause sleep-related breathing disorders such as sleep apnea (breathing pauses during sleep) and sleep-related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

Tell the doctor or pharmacist if you experience any of the following symptoms while taking **Tramadex OD**: 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.

Tell the doctor before taking this medicine if you suffer from depression and you are taking antidepressants, as some of them may interact with tramadol (see "Drug interactions").

Talk to your doctor if you are taking other medicines which may cause sedation (such as sleeping pills, medicines to treat anxiety or seizures) (see "Drug interactions").

There is a small risk that you may experience 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 "Side effects").

**This medicine should be used with caution in the case of:**

- addiction to other pain relievers (opioids)
- consciousness disorders (if you feel that you are going to faint)
- head trauma or any brain disorder such as infection or tumor
- state of shock (cold sweat may be a sign of it)
- breathing difficulties
- a history of epileptic seizures
- kidney or liver disorders
- an increase in normal brain pressure causing symptoms such as headache and vomiting (increased intracranial pressure)
- diabetes
- sensitivity to opioid class of medicines (such as pain relievers)

Epileptic fits have been reported in patients taking tramadol at the recommended dose level. The risk may be increased when doses of tramadol exceed the recommended upper daily dose limit (400 mg).

**If you are not sure, consult the doctor or pharmacist.**

**Children and adolescents**

The use of this medicine is not recommended in children under 14 years of age.

Use in children with breathing problems: tramadol is not recommended for use in children with breathing problems since the symptoms of tramadol toxicity may be worse in these children.

**Drug interactions**

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

Especially if you are taking the following medicines, because there may be drug interactions with **Tramadex OD**:

- Carbamazepine (used for the treatment of epilepsy)
- Buprenorphine, nalbuphine, pentazocine (other pain relievers)
- Alcohol
- Ondansetron (prevents nausea)

**Tramadex OD** must not be used together with monoamine oxidase (MAO) inhibitors (certain medicines used to treat depression), or if you have taken this type of medicine for the last 2 weeks (also see section 2 "Do not use the medicine").

This medicine may cause seizures at therapeutic doses and in particular when taking high doses and in combination with other medicines including:

- Bupropion (used to help stopping smoking)
- Mefloquine (a treatment for malaria)

The risk of side effects increases if you are taking:

- Other pain relievers such as morphine and codeine (also as cough medicine) or alcohol while you are taking **Tramadex OD**. You may feel drowsier or feel that you might faint. If this happens, tell the doctor.
- **Tramadex OD** and sedative medicines such as benzodiazepines or related drugs: this 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 **Tramadex OD** together with sedative medicines the dose and the duration of concomitant treatment should be limited by your doctor. The concomitant use of opioids and drugs used to treat epilepsy, nerve pain or anxiety (gabapentin and pregabalin) increases the risk of opioid overdose, respiratory depression and may be life-threatening. Tell your doctor if you are taking gabapentin or pregabalin or any sedative medicines, 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 of having a fit may increase if you are taking **Tramadex OD** at the same time. The doctor will tell you if **Tramadex OD** is suitable for you.
- Certain antidepressants. **Tramadex OD** may interact with these medicines and you may experience serotonin syndrome (see section 4 "Side effects").
- Coumarin anticoagulants (medicines for blood thinning), e.g. warfarin, together with this medicine. The effect of these medicines on blood clotting may be affected and bleeding may occur.

This medicine may also interact with the following medicines:

- Morphine-like drugs such as cough medicines or substitution treatments such as methadone
- Other pain relievers
- Benzodiazepines and other treatments for anxiety
- Some treatments for high blood pressure
- Antihistamines (for the treatment of allergies) that cause sleepiness
- Thalidomide (for the treatment of certain types of cancer and skin conditions)
- Barbiturates (sleeping pills)
- Neuroleptics, phenothiazines, butyrophenone (to treat mental illness)
- Baclofen (a muscle relaxant)
- Medicines that may inhibit certain live enzymes (such as ketoconazole and erythromycin)

### **Use of the medicine and food**

The medicine can be taken regardless of meals.

### **Use of the medicine and alcohol consumption**

Alcohol consumption is not recommended during treatment, as its effect may be intensified.

### **Pregnancy, breastfeeding and fertility**

If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, consult a doctor or pharmacist before using this medicine.

Do not take **Tramadex OD** if you are pregnant or think you might be pregnant unless you have discussed this with the doctor and the benefits of treatment are considered to outweigh the potential harm to the baby. If you use this medicine during pregnancy, your baby may become dependent and experience withdrawal symptoms after the birth which may need to be treated.

Tramadol is excreted into breast milk. For this reason, you must not take **Tramadex OD** more than once during breastfeeding. Or alternatively, if you take **Tramadex OD** more than once, you should stop breastfeeding.

Based on human experience it is thought that tramadol does not affect female or male fertility.

### **Driving and using machines**

**Tramadex OD** may cause drowsiness, dizziness and blurred vision and may therefore impair your reactions. Do not drive or do other activities requiring alertness (for example using

electric tools or operating machines), until you know how the medicine affects you. Do not take with alcohol or medicines that cause sleepiness.

The medicine can affect your ability to drive because it may cause sleepiness or dizziness. Consult the 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 less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

### **3. How to use the medicine?**

Always use the 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.

Your doctor should have discussed with you, how long the course of treatment will last and will arrange a plan for stopping treatment. This plan outlines how to gradually reduce the dose until you stop taking the medicine.

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. Do not take more than 400 mg of tramadol daily, unless your doctor has instructed you to do so.

The dosage and manner of treatment will be determined by the doctor only. The usual recommended dosage is:

#### Adults and adolescents 14 years of age and older:

The starting dosage is 100 mg, once daily. Afterwards, continue with a dosage of 200 mg, once daily. If there is not enough pain relief, the maximum dosage is 300 or 400 mg once daily.

Elderly patients (up to 75 years of age): there is no need to adjust the dosage.

Severe liver or kidney disease (insufficiency)/dialysis patients: in cases of severe liver and/or kidney insufficiency, do not take **Tramadex OD** (see also "Do not use the medicine"). If your insufficiency is mild or moderate, your doctor may recommend prolonging the dosage interval.

**Do not exceed the recommended dose.**

#### **Method of administration:**

Swallow the tablet whole with a glass of water, preferably in the evening. **Tramadex OD** can be taken with drink or food.

Do not halve, chew, crush or dissolve the tablet, as it is a prolonged release tablet. The tablets should be taken once every 24 hours.

Do not take the medicine for longer than required. If you need to be treated for a long period, the doctor will check at regular and short time intervals (including periods without treatment, if necessary) whether you can continue to take the medicine and at what dosage.

#### **If you have accidentally taken a higher dosage**

If you have taken an additional dose by mistake, this will generally have no negative effects. You should take your next dose as prescribed.

If you (or someone else) swallow a lot of this medicine at the same time, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you. Signs of an overdose include very small pupils, being sick, a fall in blood pressure, a fast heartbeat, collapse, unconsciousness, fits and breathing difficulty or shallow breathing.

#### **If you forgot to take the medicine**

If you forgot to take this medicine at the designated time, do not take a double dose to make up for a forgotten dose. Take the next dose at the regular time.

Continue with the treatment as recommended by the doctor.  
Even if there is an improvement in your health, do not stop taking this medicine without consulting the doctor.

#### **If you stop taking the medicine**

Do not suddenly stop taking the medicine. If you want to stop taking the medicine, consult the doctor first. Your doctor will tell you how to stop, usually by reducing the dose gradually so that unpleasant withdrawal effects are kept to a minimum.

Withdrawal symptoms such as restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhea, shaking, shivering or sweating may occur if you suddenly stop taking this medicine.

**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 **Tramadex OD** 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.

**If you experience any of the following side effects stop taking this medicine and proceed immediately to a doctor or a hospital emergency room.**

**Rare side effects** (effects that occur in 1-10 out of 10,000 users):

- sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body)
- fits (convulsions), especially when tramadol is taken in high doses or with medicines that induce fits
- breathing difficulties
- slow heartbeat

#### **Additional side effects**

**Very common side effects** (effects that occur in more than 1 in 10 users):

- nausea
- dizziness

**Common side effects** (effects that occur in 1-10 out of 100 users):

- constipation, dry mouth, vomiting
- sweating
- headache, drowsiness
- fatigue

**Uncommon side effects** (effects that occur in 1-10 out of 1,000 users):

- stomach trouble (a feeling of pressure in the stomach and wind), urge to be sick (retching), diarrhea
- effects on the heart and blood circulation (pounding of the heart, fast heartbeat, feeling faint or collapse). These side effects may particularly occur in patients in an upright position or under physical strain.
- skin reactions (itching, rash, hives)
- drug withdrawal syndrome

**Rare side effects** (effects that occur in 1-10 out of 10,000 users):

- muscle weakness
- changes in appetite
- abnormal sensations (e.g. itching, tingling, numbness), trembling, muscle twitches, uncoordinated movement, transient loss of consciousness (syncope), speech disorders
- increase in blood pressure
- blurred vision, excessive dilation of the pupils (mydriasis), constriction of the pupils (miosis)
- difficulty or pain in passing urine (dysuria), passing less urine than normal
- psychological complaints may appear after treatment with tramadol. Their intensity and nature may vary (according to the patient's personality and duration 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 (being less aware and less able to make decisions, which may lead to errors in judgment).
- hallucinations (seeing or hearing things), confusion, sleep disturbances, reduced awareness (delirium), anxiety, nightmares
- allergic reactions (e.g. difficulty in breathing, wheezing, swelling of skin) and shock (sudden circulation failure)
- worsening of asthma, however it has not been established whether 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.
- shortness of breath

**Very rare side effects** (effects that occur in less than 1 in 10,000 users):

- increase in liver enzymes

**Side effects with unknown frequency** (effects for which a frequency has not yet been determined):

- low levels of blood sugar
- 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, diarrhea) (see section 2 "Before using the medicine").
- drug dependence (become addicted or reliant on this medicine) may occur

### **Drug Withdrawal**

When you stop taking this medicine, you may experience drug withdrawal symptoms, which include restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhea, shaking, shivering or sweating.

### **How do I know if I am addicted?**

If you notice any of the following signs whilst taking this medicine, it could be a sign that you have become addicted:

- You need to take the medicine for longer than advised by your doctor.
- You feel you need to use more than the recommended dose.
- 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 you talk to your doctor.

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

Side effects can be reported to the Ministry of Health by clicking the link "דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website ([www.health.gov.il](http://www.health.gov.il)) directing to the online form for reporting side effects or via 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 (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 25°C.
- 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. Additional information**

**In addition to the active ingredient, the medicine also contains:**

Polyvinyl acetate, xanthan gum, hydroxypropyl distarch phosphate (E1442) (Contramid®), povidone, hydrogenated vegetable oil, magnesium stearate, silica colloidal anhydrous, sodium laurilsulfate.

**What the medicine looks like and what the package contains:**

A round, white to off-white tablet.

Approved package sizes: 2, 5, 10, 20, 30, 150 tablets. Not all package sizes may be marketed.

**Manufacturer and address:** Dexcel Ltd., 1 Dexcel St., Or Akiva 3060000, Israel.

Revised in October 2023 according to MOH guidelines.

**Drug registration number at the national drug registry of the Ministry of Health:**

**Tramadex OD 100:** 139-25-31580-00

**Tramadex OD 200:** 139-26-31581-00

**Tramadex OD 300:** 139-27-31582-00

**Registration holder:** Dexcel Pharma Technologies Ltd., 21 Haftzadi Nahum St., Jerusalem 9548402, Israel