Patient package insert according to the Pharmacists' Regulations (Preparations), 1986

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

TRAMADEX® FLASHTAB, tablets soluble in mouth, 50 mg

Active ingredient and its quantity:
Each soluble tablet contains: Tramadol Hydrochloride 50 mg.

For list of inactive ingredients, please see section 6.

Read this entire leaflet carefully before you start using this medicine.
This leaflet contains concise information about the medicine. If you have any further questions, ask the physician 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.

Do not use for treatment of children under 14 years of age.

Prescription opioids carry serious risks of addiction especially with prolonged use and they have a potential for misuse and overdose. An opioid overdose, often marked by slowed breathing, can cause death . Make sure you know the name of your medication, how much and how often to take it, the duration of treatment and its potential risks & side effects.
More information about the risks of addiction and dependence can be found at :
https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

1. What is the medicine intended for?

Tramadex Flashtab is used for the treatment of moderate to severe pain.
A non-narcotic analgesic.

Therapeutic group: Opioid analgesic.

2. Before using the medicine:

Do not use the medicine:

- If you are sensitive (allergic) to the active ingredient (Tramadol Hydrochloride), to any of the other ingredients of this medicine or to opioids.
- If you are pregnant or breastfeeding.
- If you are taking medicines belonging to the group of monoamine oxidase inhibitors (MAOI, used e.g. for the treatment of depression) or if you have taken them in the two weeks prior to starting treatment with **Tramadex Flashtab.**
- If you are in withdrawal treatment from narcotic substances or as a substitute in drug withdrawal.
- If you suffer from epilepsy and the attacks are not controlled properly by the treatment you receive.

- After consuming an amount of alcohol that made you drunk, even slightly.
- After taking medicines that slow the rate of thinking or breathing (e.g.: medicines for sleep and analgesics).
- If you are under the influence of alcohol, sedatives, sleeping pills, pain relievers (e.g.: morphine or codeine) or other psychotropic medicines (medicines that affect the mood and emotions).
- For treatment in children under 14 years of age.
- If you take nalbuphine or pentazocine (for pain relieving).
- If you take buperenorphine (e.g. for pain relieving or for the treatment of drug dependency).
- If you suffer from severe liver or renal insufficiency (creatinine clearance below 10 ml/minute).
- In patients with suicidal tendencies or a tendency for addiction or drugs/medicines or alcohol dependence.

Special warnings regarding the use of this medicine:

- **Before using Tramadex Flashtab tell your physician if:**
  - You suffer or have suffered in the past from asthma, other lung disease or breathing difficulties (a deficiency of the respiratory center or respiratory functioning).
  - You suffer or have suffered in the past from impaired function of the liver or kidney.
  - You suffer or have suffered in the past from epilepsy, convulsions or seizures, or you are at the risk for attacks (e.g. brain injury, metabolic disorder, alcohol or drug withdrawal, central nervous system infections) - the risk of attacks may increase.
  - You suffer or have suffered in the past from increased pressure on the brain due to head injury or brain disease, possible signs of this are strong headache, vomiting without feeling of nausea.
  - You used this medicine or others containing the active ingredient tramadol for a prolonged period.
  - There is a history of side effects when using the medicine or other opioid analgesics.
  - You suffer or have suffered in the past from consciousness disorders (if you feel you are about to faint).
  - You feel cold sweat, light-headed, fainting, pallor (could be signs of shock).
  - You take antidepressants, antipsychotics (for schizophrenia) or anticonvulsants (for epilepsy), tranquilizers (for the treatment of anxiety), or anti allergies that cause drowsiness.
  - You suffer from phenylketonuria – a genetic disorder characterized by the inability of the body to metabolize phenylalanine or you are sensitive to phenylketones.
  - You suffer from mental disorders or depression.
  - You suffer from sudden acute abdominal pain from unknown source – may indicate a medical emergency.
  - You are sensitive to any type of food or medicine.
  - You are at risk of respiratory depression.
  - You are over 65 years of age.

- Prolonged use may cause physical and mental dependency!
- Prolonged use may cause tolerance to the medicine - the reaction to the medicine decreases with time and therefore there is a need for larger doses.
- Do not use this medicine often or for a prolonged period without consulting a physician.
- This medicine is not intended for the relief of light pain.
- You must report to a physician that you are taking this medicine if you are about to undergo surgery or anesthesia.
- Epileptic attacks have been reported in patients who have taken tramadol in the recommended dosage. The risk might increase in a higher dosage than the maximal recommended daily dosage (400 mg).

Tell the physician or pharmacist if you are taking or have recently taken any other medicines, including non-prescription medicines and nutrition supplements.

Do not take **Tramadex Flashtab** concomitantly with:
- Medicines belonging to the group of monoamine oxidase inhibitors (MAOIs) - see section 2, sub-section "Do not use the medicine".
- Opioid analgesics e.g.: buperenorphine, pentazocine, nalbuphine - see section 2, sub-section "Do not use the medicine".

The pain relieving effect of **Tramadex Flashtab** may be reduced and the influence duration of the medicine shorter if you are taking medicines containing:
- Carbamazepine (for treatment of epileptic attacks) – concomitant use with **Tramadex Flashtab** is not recommended.
- Ondansetron (for treatment of nausea).
- Rifampicin.

The physician will direct you if you should take **Tramadex Flashtab** and in what dosage.

The risk of side effects may increase if you are taking the following medicines:
- Medicines that effect the nervous system; e.g.: phenothiazines, muscle relaxants, medicine for sleeping, sedatives, anti allergies, other analgesics such as morphine and codeine (also as a medicine for cough), alcohol, anesthetics (for surgery) or medicines for the treatment of Parkinson and epilepsy. You may feel drowsy or you may faint, if this happens - tell the physician.
- Certain antidepressants, e.g.: selective serotonin re-uptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRI), tricyclic antidepressants (TCA), monoamine oxidase inhibitors (MAOI), triptans, linezolid, lithium or the herbal medicine - St. John’s Wort might cause the "Serotonin syndrome" whose manifestations are e.g.: involuntary and rhythmic muscle contraction (including muscles that control eye movement), agitation, increased sweating, tremor, exaggeration of reflexes, increased muscle tension, fever over 38°C, confusion, muscle

spasms, diarrhea, hallucinations, coma, rapid pulse, labile blood pressure, incoordination, nausea and vomiting.
- Concomitant use with medicines that may cause seizures, e.g. antidepressants and certain antipsychotics or other opioids, might increase the chance of seizure attack. The physician will tell you if **Tramadex Flashtab** is suitable for you.
- Anticonvulsants or antiseizure medicines.
- Anti-clotting agents from the family of coumarin derivatives for blood thinning (e.g. warfarin) – their action on blood clotting might be affected and bleeding may appear.
- Quinidine, fluoxetine, paroxetine, amitriptyline, ketoconazole, erythromycin.
- Digoxin - concomitant use with **Tramadex Flashtab** may increase the risk of digoxin toxicity.
- Lithium (e.g. for treatment of manic depression)- concomitant use with **Tramadex Flashtab** may change the activity of the medicine.

Use of this medicine and food:
Food does not influence the activity of **Tramadex Flashtab**. The medicine can be taken on an empty or full stomach.

Use of this medicine and alcohol consumption:
Do not consume alcohol, do not drink wine or alcoholic beverages during the period of treatment with this medicine as its effect can increase and you might feel sleepy.

Pregnancy and breastfeeding:
Do not use **Tramadex Flashtab** if you are pregnant or breastfeeding.
There is very little information regarding the safety of using tramadol during pregnancy. Permanent use of **Tramadex Flashtab** during pregnancy can cause an addiction in the newborn and withdrawal symptoms after birth. Seizure attacks in newborns, fetal death or birth of a dead fetus have also been reported.
If you are pregnant, might be pregnant or planning to get pregnant or if you are breastfeeding - consult a physician or pharmacist before taking this medicine.

Driving and use of machinery:
Use of this medicine may cause drowsiness, dizziness and blurring of vision and therefore can impair your reactions. In such case do not drive a vehicle, operate dangerous machinery and any other activity that requires alertness. As for children, they must be warned about riding a bicycle or playing near roads etc.

Important information about some of the ingredients of this medicine:
This medicine contains aspartame, a source of phenylalanine and therefore may harm patients with phenylketonuria.

3. How to use this medicine?

- Always use according to the physician's instructions. Check with the physician or pharmacist if you are not sure.
- The dosage will be adjusted to the intensity of pain and your personal sensitivity to pain. In general, take the lowest pain relieving dosage.

The dosage and administration will be determined by the physician only.
The recommended dosage for adults and adolescents 14 years old and over:
Initial dosage of 50-100 mg (1-2 tablets). The physician may recommend a different dosage up to a maximum of 8 tablets (400 mg) daily. Wait at least 6 hours between doses, unless the physician instructs you differently.

If needed, in elderly patients (over 65 years of age), in patients with kidney and/or liver mild or moderate insufficiency, the physician might recommend lowering the dosage of the medicine and/or extending the intervals between doses.
Do not take the medicine if you suffer from severe kidney and/or liver insufficiency – see section 2, sub-section "Do not use the medicine".

Pain relief is usually attained within 30 minutes.
Do not exceed the recommended dose.

- These tablets are intended to be sucked.
- Do not halve, do not chew and do not swallow!
- If necessary, each tablet can be dissolved in half a glass of water.

Do not take this medicine for a longer time than required. If you need to be treated for a long period, the physician will check, in regular and short time intervals (with treatment intermissions, according to need), if you can continue taking the medicine and in what dosage.
If you feel that the effect of the medicine is too strong or too weak, refer to a physician or pharmacist.

If you have accidentally taken a higher dosage side effects may appear e.g.: small pupils, nausea and vomiting, weakness in skeletal muscles, cold and clammy skin, shock, arrhythmia, drop of blood pressure, rapid pulse, slow pulse, collapse, consciousness disruption and somnolence that could worsen up to stupor and coma, epileptic attacks, convulsion attacks, seizures, pulmonary edema, breathing difficulties up to apnea, shallow breathing, respiratory depression, depression of the central nervous system, cardiac arrest and death.

If you have accidentally taken a higher dosage or if a child has accidentally swallowed the medicine, proceed immediately to a physician or a hospital emergency room and bring the package of the medicine with you.

If you forgot to take this medicine at the set time, the pain might return. Do not take a double dose to compensate for the forgotten one. Take the next dose at the regular time and consult the physician.

Continue with the treatment as recommended by the physician.

Even if there is an improvement in your medical condition, do not stop the treatment with this medicine without consulting the physician or pharmacist.

If you stop taking this medicine:
If you stop or end treatment with **Tramadex Flashtab** too soon, the pain might return. If you want to stop treatment, refer to the physician. Usually, stopping treatment will have no side effects. However, certain patients may feel unwell after they stop taking the medicine. They might feel tension, instability, agitation, anxiety, panic attacks, delusions, hallucinations, illusions, paranoia, loss of identity, unusual perceptions (e.g.: itching, tingling, numbness), ringing in the ears (tinnitus), nervousness, difficulty falling asleep, difficulty sleeping, tremor, confusion, hyperactivity, stomach and bowel problems, nausea, diarrhea, abdominal cramps, anorexia, vomiting, sweating, stiffness, pain, back ache, joint pain, muscle pain, hair stands on end ("goose bumps"), tearing, runny nose, yawning, chills, pupil dilation, weakness, symptoms in the upper respiratory tract, increase in respiratory rate, increased blood pressure or increased heart rate. Other unusual manifestations in the nervous system e.g.: mania, change of perception of own personality (depersonalization), change in perception of reality (de realization). If one of these side effects appears after ceasing treatment- consult your physician.

- 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 any further questions regarding the use of this medicine, consult a physician or pharmacist.

4. Side effects:
Like any medicine, the use of **Tramadex Flashtab** may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.

Stop use of this medicine and refer to a physician immediately with the appearance of:
- An allergic reaction which includes e.g.: skin rash, swelling of the skin or face, tongue, pharynx/throat and lips, swallowing difficulties or hives together with breathing difficulty or wheezing.
- Worsening of asthma.
- Breathing difficulties.
- Convulsions (seizures).
- High fever.
- Bruising or bleeding from an unknown reason.
- Skin reactions, a severe rash with redness, peeling and swelling of the skin which is similar to severe burns (toxic epidermal necrolysis), severe form of skin rash with blushing, fever, blisters and ulcers (Stevens-Johnson syndrome).
- Shock or sudden failure in blood circulation.

Additional side effects:

Very common side effects (appear in more than 1 out of 10 users):

- Dizziness or vertigo
- Nausea, vomiting
- Constipation
- Headache
- Drowsiness
- Itching
- Stimulation of the central nervous system, the symptoms include: nervousness, anxiety, agitation, tremor, convulsions, sense of euphoria, mental instability and hallucinations
- Weakness or lack of energy
- Digestion difficulties

Common side effects (appear in 1 to 10 users out of 100):

- Dry mouth
- Sweating, excessive sweating (hyperhidrosis)
- Tiredness, weariness
- Diarrhea
- Feeling of sickness
- Expansion of blood vessels
- Confusion, coordination disturbances, pupil contraction, sleep disturbances
- Abdominal pain, anorexia, flatulence
- Increased muscle tension
- Rash
- Vision disturbances
- Symptoms of menopause in women, frequent urination, urinary retention.

Uncommon side effects (appear in 1 to 10 users out of 1,000):

- Effect on the heart and blood circulation (change of heart rate, palpitations, rapid pulse, hypotension while standing, feeling faint or collapse - these effects may occur particularly in patients in an upright position or under physical strain)
- Desire to vomit, stomach problems (feeling of pressure in stomach, feeling of bloating)

Rare side effects (appear in 1 to 10 users out of 10,000):

- Slow pulse, increased blood pressure
- Changes in appetite, unusual feelings (e.g. itching, tingling, numbness), slow breathing (if the recommended dosage is exceeded, or if taken concomitantly with other medicines that depress brain function), epileptic attacks (occurred mostly with high dosages when the medicine was taken concomitantly with other medicines that may cause attacks), muscle spasms, passing loss of consciousness (fainting), speech disorders
- Nightmares
- Delirium (acute mental confusional state, may be expressed in hallucinations, disorientation or extreme restlessness)

- Psychological complaints may appear after treatment with the medicine. Their nature and intensity may vary according to the personality of the patient and the length of treatment. These effects could appear as mood change (mostly high spirits, sometimes irritated mood), changes in activity (usually suppression, occasionally increase), decrease in function, low cognitive and sensory perception (decrease in awareness and in the ability of decision making which may lead to errors in judgment)
- Blurred vision, excessive dilation of the pupils (mydriasis)
- Shortness of breath
- Worsening of asthma has been reported although it has not been determined if caused as a result of Tramadol
- Muscle weakness
- Urinary system disorders e.g.: difficulty or pain when urinating, amount of urine which is lower than usual
- Dependency may occur if the medicine is taken for long term (though the risk for that is low)
- Extensive allergic reaction

Very rare side effects (appear in less than 1 out of 10,000 users):
- Increase in the levels of liver enzymes
- Breathing difficulties
- Flushing

Side effects with unknown frequency (effects whose frequency has not yet been determined):
- Abnormal ECG test, cardiac ischemia, pulmonary edema, pulmonary embolism
- Migraine
- Bleeding in the digestive system, liver inflammation, inflammation in the mouth, liver insufficiency
- Increase in creatinine values, hemoglobin decrease, appearance of protein in the urine
- Cataract, deafness, tinnitus (ringing in ears)
- Accidental injury, death, suicidal tendencies, weight loss, serotonin syndrome (see section 2, sub-section "Tell the physician or pharmacist if you are taking or have recently taken any other medicines, including non-prescription medicines and nutrition supplements")
- Abnormal walking, memory loss, lack of orientation and confusion, sometimes accompanied by hallucinations (delirium), depression, concentration difficulties, movement disorders
- Taste sense disturbances, pupil dilation
- Menstrual disorders
- Hypoglycemia - blood glucose (sugar) levels that are too low, characterized by e.g. muscle weakness, lack of coordination, mental confusion, sweat and in severe cases coma

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 physician.

Side effects can be reported to the Ministry of Health by clicking on the link "דיווח על תופעות לוואי עקב טיפול תרופתי""
that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form for adverse events reporting or via the following link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine, should be stored in a safe 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 physician.
- 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.
- Store below 25°C, in the original package.

6. Additional information

In addition to the active ingredient, this medicine also contains:
Mannitol, crospovidone, aspartame, ethylcellulose, mint rootbeer flavouring, copovidone, silicon dioxide, magnesium stearate.
Each mint flavored tablet contains 20 mg aspartame.

What does the medicine look like and what does the package contain:
White, round tablet, with "T" engraved on one side and "50" on the other side.

Approved package sizes: 2, 5, 7, 10, 14, 20, 28, 30, 40, 50, 56, 60, 100 tablets packed in blisters. Not all package sizes may be marketed.

Medicine registration number at the national medicines registry of the Ministry of Health: 132 15 31083 00

This leaflet was checked and approved by the Ministry of Health in February 2016.

Manufacturer and registration holder:
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