PATIENT INFORMATION LEAFLET

SCHEDULING STATUS
Schedule 5

TRAMACET Film coated tablets

Each tablet contains 37,5 mg tramadol hydrochloride and 325 mg paracetamol.

Read all of this leaflet carefully before you start taking TRAMACET

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- TRAMACET has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What TRAMACET is and what it is used for
2. What you need to know before you take TRAMACET
3. How to use TRAMACET
4. Possible side effects
5. How to store TRAMACET
6. Contents of the pack and other information

1. What TRAMACET is and what it is used for

Tramadol and paracetamol are the active substances in TRAMACET. They are painkillers that act on the brain and spinal cord to control pain. TRAMACET is used for the management of moderate to moderately severe pain in adults.

2. What you need to know before you take TRAMACET

Do not take TRAMACET if:

- if you are hypersensitive (allergic) to tramadol or paracetamol or to any other opioid or any of the other ingredients of TRAMACET (listed in section 6);
- if you take other medicines containing paracetamol or tramadol;
- if you have a severe liver disease;
- if you are taking alcohol;
- if you are taking sleeping pills;
- if you are taking other psychotropic medicines (medicines that affect mood and emotions);
- if you are taking MAO inhibitors (certain medicines used for depression) or have taken them in the last 14 days before treatment with TRAMACET;
- 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 epilepsy or suffer from seizures;

- Do not give TRAMACET to a child under 12 years of age;

- Do not give TRAMACET to a child under 18 years of age that has just had an operation to remove their tonsils or adenoids.

Warnings and precautions

Take special care with TRAMACET

- Do not take more than your recommended dose;
- Tell your doctor if you have ever had an allergic reaction (characterised by significant skin rash, itching, hives, difficulty breathing, and/or swollen face) while taking codeine or other opioids;
- Tell your doctor if you are taking other medicines which contain tramadol or paracetamol;
- Tell your doctor if you have fits (seizures);
- Tell your doctor if you are taking any other medicine, because taking some medicines together with TRAMACET may increase your risk of fits (seizures);
- Tell your doctor if you use sedatives, tranquilisers, sleeping pills, medicines for pain relief, anaesthetics or if you drink alcohol;
- Tell your doctor if you have recently suffered from a head injury or severe headaches associated with vomiting;
- If you suffer from increased pressure in the brain (possibly after a head injury or brain disease);
- Tell your doctor if you are dependent on any opioid painkillers;
- Tell your doctor if you are dependent on alcohol or have a history of alcohol abuse;

- Tell your doctor if you want to stop taking TRAMACET. You may become dependent on TRAMACET and may need to reduce the dose of TRAMACET slowly to avoid withdrawal symptoms;

- Tell your doctor if you know you have a kidney disorder. The dose of TRAMACET may need to be adjusted;
- Tell your doctor if you know you have a liver problem. TRAMACET may not be recommended for you;

- Stop taking TRAMACET and tell your doctor immediately if you experience skin rash, especially:
    - A red rash covered with small pus-filled bumps that can spread over the body, sometimes with a fever (acute generalised exanthematous pustulosis);
    - A life-threatening rash with blisters and peeling skin over much of the body (toxic epidermal necrolysis);
    - A severe rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome);
- Tramadol works by being converted (metabolised) into its active component. Some patients convert (metabolise) tramadol to this active component more rapidly and completely than other patients. These patients are more likely to have serious side effects, such as breathing difficulties, with slow or shallow breathing. If you experience these types of side effects, stop taking TRAMACET and consult with your doctor immediately.
- Some patients taking TRAMACET may experience low levels of sodium in the blood (hyponatraemia). Symptoms of low blood sodium may include nausea and vomiting, headaches, feeling confused, feeling very tired, feeling restless,

feeling irritable, muscle weakness, spasms or cramps and seizures. Elderly patients and patients taking other medicines that lower sodium in the blood are most at risk for this side effect. If you get any of these symptoms while taking TRAMACET, consult with your doctor immediately.

- TRAMACET can cause low levels of oxygen in the blood and a problem called sleep apnoea (stopping breathing from time to time whilst sleeping). Tell your doctor if you have a history of sleep apnoea or if anyone notices you stop breathing from time to time whilst sleeping.

This product contains paracetamol and is fatal in overdose.

In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or poison centre must be contacted immediately.

Children

- TRAMACET is not for use in children under 12 years old as it may result in breathing difficulties, with slow or shallow breathing, that could lead to death.

Other medicines and TRAMACET:

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

In particular, tell your doctor or pharmacist if you are taking any of the following medicines as TRAMACET may affect how well they work:

- Monoamine Oxidase Inhibitors (MAOIs) or Selective Serotonin Reuptake Inhibitors (SSRI's), used to treat depression or Parkinsons Disease;
- Medicines used to treat depression, e.g. mirtazapine, tricyclic antidepressants, trazadone;
- Triptans, used to treat migraines;
- 5-HT3 receptor antagonists, used to treat nausea and vomiting;
- Medicines that slow down your central nervous system (CNS depressants) such as sedatives, sleeping pills, medicines for surgery (anaesthetics), tranquilisers (benzodiazepines), medicines used to treat certain mental conditions (psychotropic medicines), some strong painkillers (opioids), or alcohol;
- Carbamazepine, used to treat epilepsy and some types of pain;
- Phenytoin, used to treat seizures,
- Quinidine, used to treat heart conditions (antiarrhythmics);
- Warfarin like compounds, used to stop blood clotting (blood thinners);
- Medicines that slow or reduce the conversion (metabolism) of this medicine to its active form (CYP2D6 inhibitors);
- Cimetidine, used to treat heart burn and peptic ulcers;
- Antibiotics to treat infections, e.g. erythromycin, rifampin, linezolid;
- Antifungals used to treat fungal infections, e.g. ketoconazole;
- Anti-retrovirals used to treat HIV/AIDs, e.g. ritonavir;
- Diflunisal, may elevate paracetamol plasma levels.

TRAMACET with food and drink

Do not drink alcohol during treatment with TRAMACET as the effects of TRAMACET and alcohol may intensify each other.

You may take TRAMACET at any time of the day with or without food.

Pregnancy and Breastfeeding:

The safe use of TRAMACET has not been demonstrated in pregnant and breastfeeding women. TRAMACET is thus not recommended for pregnant and breastfeeding mothers, as small amounts of tramadol may pass into breast milk.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking TRAMACET.

Opioid medicines can slow the breathing of a newborn child.

Prolonged use of TRAMACET during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognised and treated. The risk is increased in the last trimester of pregnancy.

Driving and using machines

TRAMACET may make you feel tired, dizzy or drowsy. Do not drive a car or operate machinery while taking TRAMACET.

3. How to take TRAMACET

Do not share medicines prescribed for you with any other person.

Always take TRAMACET exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

TRAMACET comes in the form of a tablet to be taken by mouth.

Do not take more than the recommended dose of TRAMACET. The lowest effective dose should be used for the shortest period of time.

The usual dose is:

Adults (including elderly) and children over 16 years of age:

Take 1 or 2 tablets every 4 to 6 hours as needed for pain relief up to a maximum of 8 tablets per day.

TRAMACET should not be given to children under 16 years of age.

Patients with kidney or liver impairment

Do not take TRAMACET if you have severe liver problems.

Tell your doctor if you have a kidney disorder (a creatinine clearance < 30 mL/min). Do not take more than 2 tablets every 12 hours.

DO NOT TAKE MORE THAN THE RECOMMENDED DOSE.

Your doctor will tell you for how long your treatment with TRAMACET will last. If you have the impression that the effect of TRAMACET is too strong or too weak, tell your doctor or pharmacist.

If in doubt, ask your doctor or pharmacist.

If you take more TRAMACET than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre. Even if you feel well after having taken more TRAMACET than you should have, you should still seek medical assistance as there is a risk of delayed, serious liver damage.

Breathing difficulties with slow or shallow breathing and/or fits (seizures), irritation and discomfort in the stomach and gut, loss of appetite, nausea, vomiting, feeling unwell, unusually pale colour and sweating. Cases of abnormal electrical conduction in the heart (QT prolongation) have been reported.

Your doctor will take the necessary measures.

If you forget to take TRAMACET

The pain is likely to return. Do not take a double dose to make up for the forgotten individual doses, simply continue taking the tablets as before.

4 Possible side effects

TRAMACET can have side effects.

Not all side effects reported for TRAMACET are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while taking TRAMACET, please consult your doctor, pharmacist or other health care professional for advice.

Frequent side effects of TRAMACET

- Nausea;
- Dizziness;
- Headache;
- Muscle tremor;
- Stomach pain;
- Constipation;
- Diarrhoea;
- Indigestion;
- Passing wind;

- Dry mouth;
- Vomiting;
- Loss of appetite;
- Feeling anxious;
- Feeling confused;
- Feeling extremely happy (euphoria);
- Feeling sleepy;
- Feeling nervous;
- Feeling weak;
- Feeling very tired;
- Hot flushes;
- Itching;
- Rash;
- Increased sweating;
- High blood pressure;
- High blood pressure that is worse than before;
- Low blood pressure;
- Abnormal heart rhythm;
- Heart beat feels fast;
- Fast heart beat;
- Changes that show up in blood tests of the liver;
- Loss of coordination;
- Fits;
- Abnormal muscle tension;
- Migraine;
- Migraines that are worse than before;
- Muscle twitching;

- Unusual feeling in the skin (such as tingling or a crawling feeling);
- Decreased consciousness;
- Spinning sensation (vertigo);
- Difficulty swallowing;
- Black tarry stools;
- Swelling of the tongue;
- Persistent ringing in the ears;
- Weight loss;
- Loss of memory;
- Feeling detached from yourself;
- Depression;
- Drug abuse;
- Mood swings;
- Seeing, feelings, hearing or smelling things that are not there (hallucinations);
- Difficulty getting and keeping an erection (impotence);
- Bad dreams;
- Abnormal thinking;
- Low number of red blood cells (anaemia);
- Being short of breath;
- Protein in the urine (albuminuria);
- Problems passing urine;
- Passing less urine than usual;
- Being unable to pass urine or empty the bladder completely;
- Problems with vision.

Less Frequent side effects of TRAMACET:

- Confusional state;
- Excessive contraction of the pupil of the eye;
- Prolonged dilatation of the pupil of the eye;
- Speech disorder;
- Movement disorder;
- Low blood sugar. (Most cases were in patients who had existing risk factors such as diabetes, kidney disease or in elderly patients);
- Low levels of sodium in the blood and/or inappropriate antidiuretic hormone secretion (SIADH).

Side effects of tramadol hydrochloride:

- Feeling dizzy upon sitting up or standing up;
- Allergic reactions including:
    - a severe allergic reaction that may include:
        - a swollen face, lips, mouth, tongue or throat;
        - difficulty swallowing or breathing;
        - itchy rash (hives);
    - hives;
    - severe rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome);
    - life-threatening rash with blisters and peeling skin over much of the body (toxic epidermal necrolysis);
- Difficulty thinking, remembering information, or solving problems;
- Thoughts of harming or killing yourself;
- Inflamed liver;
- Increased level of creatinine in the blood;

- Life-threatening increases of 'serotonin' in the brain (serotonin syndrome), which may lead to:
  - feeling confused or restless;
  - sweating, shivering, muscle jerks, fast heart beat,

    particularly if you take other medicines used to treat depression such as Monoamine Oxidase Inhibitors (MAO inhibitors) or Selective Serotonin Reuptake inhibitors (SSRI's) at the same time as TRAMACET;
- Severe confusion;
- Constricted pupils;
- Dilated pupils;
- Speech problems;
- Problem being able to produce or control movement;
- Changes in the effects of blood thinners (such as warfarin) including an increase in prothrombin time, causing an increased risk of bleeding;
- Low level of sugar in the blood;
- Low level of sodium in the blood.

Side effects of paracetamol:

- Allergic reactions (skin rash);
- Allergic reaction to paracetamol;
- Low level of 'prothrombin' in the blood, causing an increased risk of bleeding when taken with blood thinners.
- Red and swollen skin that may blister

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of TRAMACET.

5. How to store TRAMACET

Keep TRAMACET in a cool, dry place, at or below 30 °C.

Do not remove the blisters from the carton until required.

Store all medicines out of reach of children.

Protect from light and moisture.

Do not use after the expiry date stated on the label.

Store this medicine securely, where other people cannot access it. It may harm people who may take this medicine by accident, or intentionally when it has not been prescribed for them.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What TRAMACET contains

The active ingredients in TRAMACET are 37,5 mg tramadol hydrochloride and 325 mg paracetamol.

The other ingredients are: carnauba wax, hypromellose, iron oxide, magnesium stearate, maize starch, polyethylene glycol, polysorbate 80, powdered cellulose, pregelatinised starch, sodium starch glycolate and titanium dioxide.

What TRAMACET looks like and contents of the pack

Light yellow, film-coated capsule-shaped tablet engraved “J-C” on one side and “T/P” on the other.

Clear, colourless PVC blister packs of 60 tablets. The blisters are packed in cartons containing 6 strips of 10 tablets each.

Holder of Certificate of Registration

JANSSEN PHARMACEUTICA (PTY) LTD

(Reg. No. 1980/011122/07)

2 Medical Road, Halfway House

Midrand, 1685

Tel: +27 (0)11 518 7000

MedInfoZa@its.jnj.com

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Registration numbers

TRAMACET: 35/2.9/0010

Access to the corresponding Professional Information:

Included in the carton, accompanying this patient information leaflet.