Patient Information Leaflet:

TRAMADOL 50MG/ML SOLUTION FOR INJECTION OR INFUSION

(referred to as Tramadol Injection throughout this leaflet)

Please read all of this leaflet carefully before being given Tramadol Injection, because it contains important information for you.

- Keep this leaflet as you may need to refer to it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any Possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. WHAT TRAMADOL INJECTION IS AND WHAT IT IS USED FOR

Tramadol belongs to a group of medicines known as analgesics or "pain-killers". Tramadol is used to relieve pain and can also be used to prevent pain.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN TRAMADOL INJECTION

You must NOT be given Tramadol Injection and you should talk to your doctor immediately:

- If you are allergic to tramadol hydrochloride or any of the other ingredients of the solution. Allergic reactions to tramadol could include skin rash, swelling of the face, wheezing or difficulty breathing
- If you are epileptic and your fits are not well controlled by treatment
- If the patient is a child under 12 years of age
- If you are pregnant or breast-feeding
- If you are taking any of the following medicines:
  - sleeping tablets or tranquillizers such as nitrazepam
  - other pain-killers such as codeine or morphine
  - psychotropic medicines such as chlorpromazine
  - a monoamine oxidase inhibitor used to treat depression, or if you have taken one in the past two weeks
- If you have recently been drinking alcohol.

It should not be used in narcotic drug withdrawal treatment.

Tell your doctor before you are given Tramadol Injection:

- If you have liver or kidney disease. You may need a lower dose or a longer interval between doses
- If you have a head injury or brain disease
- If you have a problem that makes you faint or feel faint
- If you are in a state of shock. You may feel light headed, faint, cold or clammy or look pale
- If you suffer from epilepsy, convulsions or seizures (fits) or have had them in the past
- If you suffer from asthma, other lung diseases or have difficulty in breathing.
- If you think you may be addicted to other pain relievers (opioids)

Tramadol may lead to addiction.
In patients with a tendency to drug abuse, Tramadol Injection should only be given for short periods under strict medical supervision.Tramadol is transformed in the liver by an enzyme. Some people have a variation of this enzyme and this can affect people 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, you must stop taking this medicine and seek medical advice: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation, lack of appetite.
Use 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.

Other medicines and Tramadol

Tell your doctor if you are taking, or have recently taken, any of the following medicines. This is important because Tramadol Injection could alter how other medicines work.

- Serotonin – norepinephrine reuptake inhibitors (SNRI's) tricyclic antidepressants, antipsychotics and other seizure threshold-lowering medicinal products (such as bupropion, mirtazapine, (tetrahydrocannabinol) to cause convulsions.
- carbamazepine, a treatment for epilepsy, as this may reduce the effectiveness of the tramadol
- triptans, such as sumatriptan, used to treat migraines, as this may increase the effectiveness of the triptans
- coumarin anticoagulants, used to thin the blood, such as warfarin, as this may alter the effectiveness of the anticoagulant
- selective serotonin reuptake inhibitors (SSRI's), used to treat depression, such as fluoxetine, as this may increase the effect of the SSRI's
- lithium, used to treat psychotropic disorders, as this may alter the effect of lithium
- ondansetron, used to prevent nausea and vomiting.

Other active substances known to inhibit CYP3A4, such as ketoconazole and and erythromycin, might inhibit the metabolism of Tramadol.The concomitant use of opioids with sedating medicinal products such as benzodiazepines or related products increases the risk of respiratory depression, sedation, coma and death because of additive CNS depressant effect. The dose of Tramadol and the duration of the concomitant use should be limited.

Tell your doctor if you are taking, have recently taken or might take any other medicines.
The risk of side effects increases

- if you are taking medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk of having a fit may increase if you are given Tramadol Injection at the same time. Your doctor will tell you whether Tramadol Injection is suitable for you.
- if you are taking certain antidepressants. Tramadol Injection may interact with these medicines and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38 °C.

This medicinal product contains less than 1 mmol sodium (1.4mg) per 2ml dose i.e. essentially 'sodium free'

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. There is very little information on the safety of tramadol in pregnancy, therefore Tramadol Injection should not be used if you are pregnant.
Chronic use during pregnancy may lead to withdrawal symptoms in newborns.
Tramadol is excreted into breast milk. For this reason, you should not take tramadol injection more than once during breast-feeding, or alternatively, if you take tramadol injection more than once, you should stop breast-feeding.

Driving and using machinery

Tramadol Injection may cause drowsiness, dizziness or blurred vision, these effects may be increased by alcohol and other depressants. Do not drive or use machinery if you are affected. The medicine can affect your ability to drive as it may make you sleepy or dizzy

Continued overleaf…

Information for the Healthcare Professional

Tramadol 50mg/ml Solution for Injection or Infusion Please read this information carefully before using Tramadol 50mg/ml Solution for Injection or Infusion (referred to as Tramadol Injection). Further information is contained in the Summary of Product Characteristics. Presentation.

Tramadol Injection is presented as a clear colourless solution in a neutral glass ampoule. Each ampoule contains 2ml of tramadol hydrochloride 50mg/ml.

Dosage and Method of Administration

Whenever solution and container permit, parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration. Only a clear solution should be used. Tramadol Injection is for parenteral injection either intramuscularly, by slow intravenous injection or diluted in solution for administration by infusion or patient controlled analgesia. The dose should be adjusted to the intensity of the pain and the sensitivity of the individual patient. The lowest effective dose for analgesia should generally be selected. The total daily dose of 400mg tramadol hydrochloride should not be exceeded, except in special clinical circumstances. Tramadol Injection should not be given for longer than absolutely necessary. If long term pain treatment is necessary then careful regular monitoring should be carried out, with breaks in treatment if necessary.

Adults and Children over 12 years

The usual dose is 50 or 100mg 4 to 6 hourly by either intramuscular or intravenous routes. Intravenous injections must be given slowly over 2–3 minutes. The dose should be adjusted according to the severity of the pain and the response. For post-operative pain, an initial bolus of 100mg is administered. During the 60 minutes following the initial bolus, further doses of 50mg may be given every 10-20 minutes, up to a total dose of 250mg including the initial bolus. Subsequent doses should be 50mg or 100mg 4-6 hourly up to a total daily dose of 400mg.

Elderly

A dose adjustment is not usually necessary in patients up to 75 years without clinically manifest hepatic or renal insufficiency. In elderly patients over 75 years elimination may be prolonged. Therefore, if necessary the dosage interval is to be extended according to the patient's requirements.

- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
  - o The medicine has been prescribed to treat a medical or dental problem and
  - o You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
  - o It was not affecting your ability to drive safely

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

3. HOW TRAMADOL INJECTION SHOULD BE GIVEN

Your doctor or nurse will usually give you Tramadol Injection. The solution may be given by an injection into either a vein or muscle. If you are in hospital you may receive tramadol through a drip (infusion) or from a small machine that allows you to have tramadol when you need it by pushing a button. The doctor or nurse will explain how to use the machine.
The usual dose is one injection of 50mg or 100mg every 4 to 6 hours. After an operation you may need injections more often. Elderly patients: 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 should not be given Tramadol Injection. If in your case the insufficiency is mild or moderate, your doctor may recommend prolonging the dosage interval.
Tramadol Injection should not be given to children under 12 years of age.
The dosage should be adjusted to the intensity of your pain and your individual pain sensitivity.
In general, the lowest dose to relieve pain should be given for the shortest possible time.

If you receive too much Tramadol Injection.
If you think you have been given or have given yourself too much Tramadol Injection, tell a doctor or nurse immediately. Symptoms of intoxication are similar to those of other centrally acting analgesics (opioids) are to be expected. These include in particular miosis, vomiting, cardiovascular collapse, consciousness disorders up to coma, convulsions and respiratory depression up to respiratory arrest.

If you stop receiving Tramadol Injection
You should not suddenly stop taking this medicine unless your doctor tells you to. If you want to stop taking your medicine, discuss this with your doctor first, particularly if you have been taking it for a long time. Your doctor will advise you when and how to stop, which may be by lowering the dose gradually to reduce the chance of developing unnecessary side effects (withdrawal symptoms). Rarely when some people stop treatment with tramadol they get withdrawal symptoms. These symptoms include agitation, anxiety, nervousness, insomnia, hyperkinesia, tremor and gastrointestinal symptoms. Other symptoms that have rarely been seen with Tramadol discontinuation include: panic attacks, severe anxiety, hallucinations, paraesthesias, tinnitus and unusual CNS symptoms (i.e. confusion, delusions,personalization, derealisation, paranoria).

4. POSSIBLE SIDE EFFECTS

Like all medicines, Tramadol Injection can cause side effects. However, do not be alarmed, as most patients do not have problems with this medicine.

Tell your doctor or a nurse immediately if you experience any of the following:
- swelling around the throat, tightness in your chest or difficulty in breathing.

You may have had an allergic reaction, these are rare but, if severe, can be serious and you may need urgent medical attention.

Tell a doctor or nurse if you get any of the following other side effects:
Very common side effects (occurring in more than 1 in 10 patients):
- nausea, dizziness

Common side effects(occurring in less than 1 in 10 patients):
- headache, drowsiness, fatigue
- vomiting, constipation, dry mouth, sweating.

Uncommon side effects (occurring in less than 1 in 100 patients):
- changes in heart beat or rhythm which may make you feeling faint or dizzy especially if you stand up quickly
- retching, stomach irritation or feeling bloated
- diarrhoea
- dermal reactions – rash, itching, hives.

Rare side effects (occurring in less than 1 in 1000 patients):
- changes in appetite, abnormal touch sensations, trembling, difficulty breathing, fits, fainting, speech disorders
- slowing of the heart rate, increased blood pressure
- nightmares, disturbed sleep patterns, hallucinations (seeing things), feeling confused, changes in mood, activity or awareness, anxiety, delirium
- blurred vision, excessive dilation or constriction of the pupils
- muscle weakness or twitching, abnormal coordination
- increase in liver enzymes
- difficulty or pain passing water (urine)
- worsening of asthma, shortness of breath
- Rarely when some people stop taking tramadol they get withdrawal symptoms. These symptoms include agitation, nervousness, shaking, hyperactivity and difficulty in sleeping.

Very rarely panic attacks, severe anxiety, hallucinations, tinnitus or abnormal skin sensations, as well as confusion, delusions, personalisation, derealisation and paranoia, have occurred.

Other side effects (frequency unknown):
- low blood sugar levels.
- hypoglycaemia

Reporting of side effects
If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search MHRA Yellow Card on the Google Play or Apple App store. By reporting side effects you can help provide more information on the safety of this medicine.

5. STORING TRAMADOL INJECTION

The hospital will store the medicines. Keep out of reach and sight of children.This medicinal product does not require any special storage conditions. Keep ampoule in the outer carton. Do not use this product if there are signs of damage to the ampoule or if the solution is cloudy or contains particles. Tramadol Injection should not be used after the 'use by' date on the carton.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What is in this medicine:
Each 2 ml ampoule contains 100mg of tramadol hydrochloride.The ampoules also contain sodium acetate trihydrate and water for injections.
What this medicine looks like and contents of the pack:
Tramadol Injection is a clear colourless solution. Each pack contains 5 glass ampoules
Marketing authorisation holder: Beacon Pharmaceuticals Ltd., DCC Vital, Westminster Industrial Estate, Repton Road, Measham, DE12 7DT, England.
Manufacturer: Biologici Italia Laboratories S.r.l., Via F. Serpero, 2 – 20060 Masate (MI), Italy.
This leaflet does not include all the information about this medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.
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Beacon PHARMACEUTICALS

Renal insufficiency/dialysis and hepatic impairment
In patients with renal and/or hepatic insufficiency the elimination of tramadol is delayed. In these patients prolongation of the dosage intervals should be carefully considered according to the patient's requirements.
Children under 12 years Not recommended. **Contraindications** Tramadol Injection should not be given to patients who have previously demonstrated hypersensitivity towards tramadol or any of the other ingredients in this medicine. Tramadol Injection should not be given to patients suffering from acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids or psychotropic drugs. In common with other opioid analgesics, tramadol should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal. Tramadol Injection is contraindicated in patients with epilepsy not adequately controlled by treatment. Tramadol must not be used in narcotic withdrawal treatment.
Pharmaceutical Information
Excipients Sodium acetate trihydrate and Water for Injections.

Incompatibilities Precipitation will occur if Tramadool injection is mixed in the same syringe with injections of diazepam, diclofenac sodium, indomethacin, midazolam and piroxicam.
Shelf-life 3 years
Storage Precautions Keep ampoule in the outer carton. This medicinal product does not require any special storage conditions.
Nature of Container 2ml neutral glass type I glass ampoules for injections. Box of 5 ampoules.
Instructions for Use and Handling. The prepared infusion solution should be made up immediately before use. Tramadol Injection is physically and chemically compatible for up to 24 hours with 4.2% sodium bicarbonate and Ringer's solution; and for up to 5 days with the following infusion solutions:
- 0.9% sodium chloride
- 0.18% sodium chloride and 4% glucose
- sodium lactate compound
- 5% glucose