1. NAME OF THE MEDICINAL PRODUCT

Habitram 50mg/ml Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Tramadol Hydrochloride BP…….50mg

Water for injection BP……..q.s

3. PHARMACEUTICAL FORM

Solution for Injection

Clear, colorless sterile solution for injection or infusion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Tramadol is a strong pain medication used to treat moderate to severe pain that is not being relieved by other types of pain medicines. Tramadol is a synthetic opioid and acts in the brain and spine (central nervous system) to reduce the amount of pain you feel.

4.2 Posology and method of administration

Posology

Adults and Children above 12 Years of age

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. A dose adjustment is not usually necessary in elderly 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.

Dosage recommendations:
The usual dose is 50 or 100mg 4-6 hourly by the intravenous or intramuscular route. Dosage should be adjusted according to pain severity and response.

Intravenous injections must be given slowly over 2-3 minutes.

For post-operative pain administer an initial bolus of 100mg. 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.

Children

Tramadol hydrochloride 50 mg/ml solution for injection or infusion is not suitable for children below the age of 12 years.

Geriatric patients

A dose adjustment is not usually necessary in elderly 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.

Renal Insufficiency/Dialysis and Hepatic Insufficiency

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.

Method of administration

Route of administration by infusion or patient controlled analgesia

Contraindications

Tramadol hydrochloride 50 mg/ml solution for injection or infusion is contraindicated

- In patients who have previously shown hypersensitivity to the active substance tramadol or to any of the excipients listed in section 6.1.

- In patients suffering from acute intoxication with alcohol, hypnotics, analgesics, opioids, or psychotropic medicinal products.

- In patients who are receiving monoamine oxidase (MAO) inhibitors or who have taken them within the last 14 days.

- In patients with epilepsy not adequately controlled by treatment.

- For use in narcotic withdrawal treatment.

4.3 Special warnings and precautions for use

Tramadol hydrochloride 50 mg/ml solution for injection or infusion may only be used with particular caution in opioid-dependent patients, patients with head injury, shock, a reduced level of consciousness of uncertain origin, disorders of the respiratory centre

or function, increased intracranial pressure.

In patients sensitive to opiates the product should only be used with caution.

Care should be taken when treating patients with respiratory depression, or if concomitant CNS depressant drugs are being administered (see section 4.5), or if the recommended dosage is significantly exceeded (see section 4.9) as the possibility of respiratory depression cannot be excluded in these situations.

Convulsions have been reported in patients receiving tramadol at the recommended dose levels. The risk may be increased when doses of Tramadol exceed the recommended upper daily dose limit (400 mg). In addition, tramadol may increase the seizure risk in patients taking other medicinal products that lowers the seizure threshold (see section 4.5). Patients with epilepsy or those susceptible to seizures should only be treated with tramadol if there are compelling circumstances.

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs

Concomitant use of Tramadol hydrochloride 50 mg/ml solution for injection or infusion and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Tramadol hydrochloride 50 mg/ml solution for injection or infusion concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

Sleep-related breathing disorders

Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

Adrenal insufficiency

Opioid analgesics may occasionally cause reversible adrenal insufficiency requiring monitoring and glucocorticoid replacement therapy. Symptoms of acute or chronic adrenal insufficiency may include e.g. severe abdominal pain, nausea and vomiting, low blood pressure, extreme fatigue, decreased appetite, and weight loss.

Drug dependence, tolerance and potential for abuse

For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals

with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over- the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance.

The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction. The clinical need for analgesic treatment should be reviewed regularly.

Drug withdrawal syndrome

Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with Tramadol hydrochloride 50 mg/ml solution for injection or infusion.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

Tramadol hydrochloride 50 mg/ml solution for injection or infusion is not a suitable substitute in opioid dependent patients. Although it is an opioid agonist, tramadol cannot suppress morphine withdrawal symptoms.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

Hyperalgesia

Hyperalgesia may be diagnosed if the patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain

related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

CYP2D6 metabolism

Tramadol is metabolised by the liver enzyme CYP2D6. If a patient has a deficiency or is completely lacking this enzyme an adequate analgesic effect may not be obtained. Estimates indicate that up to 7% of the Caucasian population may have this deficiency. However, if the patient is an ultra-rapid metaboliser there is a risk of developing side effects of opioid toxicity even at commonly prescribed doses.

General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life threatening and very rarely fatal. Post-operative

Use in children

There have been reports in the published literature that tramadol given post-operatively in children after tonsillectomy and/or adenoidectomy for obstructive sleep apnoea, led to rare, but life threatening adverse events. Extreme caution should be exercised when tramadol is administered to children for post-operative pain relief and should be accompanied by close monitoring for symptoms of opioid toxicity including respiratory depression.

Children with compromised respiratory function

Tramadol is not recommended for use in children in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of opioid toxicity.

Serotonin syndrome

Serotonin syndrome, a potentially life-threatening condition, has been reported in patients receiving Tramadol in combination with other serotonergic agents or tramadol alone (see sections 4.5, 4.8 and 4.9).

If concomitant treatment with other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose escalations.

Symptoms of serotonin syndrome may include mental status changes, autonomic instability, neuromuscular abnormalities and/or gastrointestinal symptoms.

If serotonin syndrome is suspected, a dose reduction or discontinuation of therapy should be considered depending on the severity of the symptoms. Withdrawal of the serotonergic drugs usually brings about a rapid improvement.

4.4 Interaction with other medicinal products and other forms of interaction

Caution should be exercised during concomitant treatment with tramadol and coumarin derivatives (e.g. warfarin) due to reports of increased INR with major bleeding and ecchymoses in some patients.

4.5 Pregnancy and lactation

Pregnancy

Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate.

If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available. Tramadol - administered before or during birth - does not affect uterine contractility.

Animal studies with tramadol revealed at very high doses effects on organ development, ossification and neonatal mortality. Tramadol crosses the placenta. There is inadequate evidence available on the safety of tramadol in human pregnancy. Therefore Tramadol hydrochloride 50 mg/ml solution for injection or infusion should not be used in pregnant women.

Breast-feeding

Approximately 0.1 % of the maternal dose is excreted into the milk. In the immediate post-partum period, for maternal oral daily dosage up to 400 mg, this corresponds to a mean amount of tramadol ingested by breast-fed infants of 3% of the maternal weight-adjusted dosage. For this reason administration to nursing women is not recommended as tramadol may be secreted in breast milk and may cause respiratory depression in the infant. Alternatively, breast-feeding should be discontinued during treatment with tramadol.

Fertility

Post marketing surveillance does not suggest an effect of tramadol on fertility. Animal studies did not show an effect of tramadol on fertility.

4.6 Effects on ability to drive and use machines

Tramadol hydrochloride 50 mg/ml solution for injection or infusion may cause effects such as somnolence and dizziness and therefore may impair a patient's ability to drive safely or operate machinery. This applies particularly in conjunction with alcohol and other psychotropic substances. Patients should, therefore, not drive or operate machinery.

4.7 Undesirable effects

4.8.1 General

Rapid intravenous administration may be associated with a higher incidence of adverse effects and therefore should be avoided.

The most commonly reported adverse drug reactions are nausea and dizziness, both occurring in more than 10% of patients.

The frequencies are defined as follows:

Very common: ≥1/10, Common: ≥1/100, <1/10, Uncommon: ≥1/1000, <1/100, Rare: ≥1/10 000, <1/1000, Very rare: <1/10 000

Not known: cannot be estimated from the available data

Table of Adverse Drug Reactions

System Organ Class	Frequency Classification	Adverse Drug Reaction
Cardiovascular disorders	Rare	bradycardia
Vascular disorders	Rare	changes in appetite
Respiratory, thoracic and mediastinal disorders	Rare	*R*espiratory depression, dyspnoea
Nervous system disorders	Rare	Changes in appetite, paraesthesia, tremor, respiratory depression, epileptiform convulsions, involuntary muscle contractions, abnormal coordination, syncope.
Psychiatric disorders	Rare	hallucinations, confusion, sleep disturbance, delirium, anxiety and nightmares
Eye disorders	Rare	miosis, mydriasis, blurred vision
Gastrointestinal disorders	Very common	nausea
Skin and subcutaneous tissue disorders	Common	sweating
Musculoskeletal and connective tissue disorders	Rare	motorial weakness
Hepatobiliary disorders	Common	increase in liver enzyme

		values
Renal and urinary disorders	Rare	micturition disorders (difficulty in passing urine, dysuria and urinary retention)
Immune system disorders	Rare	allergic reactions (e.g. dyspnoea, bronchospasm, wheezing, angioneurotic oedema) and anaphylaxis
General disorders and administration site conditions	Uncommon	drug withdrawal syndrome

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.8 Overdose

On intoxication with tramadol symptoms 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Analgesic, ATC code: N02AX02

Tramadol also has an antitussive action. At the recommended dosages, the effects of tramadol given orally on the respiratory and cardiovascular systems appear to be clinically insignificant. The potency of tramadol is reported to be 1/10th to 1/6th that of morphine.

5.2 Pharmacokinetic properties

The inhibition of one or both cytochrome P450 isoenzymes, CYP3A4 and CYP2D6 involved in the metabolism of tramadol, may affect the plasma concentration of tramadol or its active metabolite.

Tramadol is essentially excreted via the kidneys. The mean elimination half-life of tramadol following intravenous administration is 5-6 hours. Total clearance of tramadol was 28.0 L/h following intravenous administration.

5.3 Preclinical safety data

Tramadol Hydrochloride is a well – established active ingredient.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Precipitation will occur if Tramadol hydrochloride 50 mg/ml solution for injection or infusion is mixed in the same syringe with injections of diazepam, diclofenac sodium, indomethacin, midazolam and piroxicam.

6.3 Shelf life

36 Months from the date of manufacturing.

6.4 Special precautions for storage

Store in a cool dry place below 30°C. Protect from light.

6.5 Nature and contents of container and special equipment for use, administration orimplantation

Colourless glass ampoule containing either 1 ml or 2 ml of injection solution. Ampoules are contained in a pre-fabricated blister strip, which is enclosed in a cardboard outer carton. Cartons contain either 1, 5 or 10 ampoules.

6.6 Special precautions for disposal and other handling

The prepared infusion solution should be made immediately before use.

7. MARKETING AUTHORIZATION HOLDER

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08/10/2025

10. DATE OF REVISION OF THE TEXT

10/2025