September 2019

Tramal Injection 100

רופא/ה, רוקח/ת נכבד/ה,

חברת טק-או-פארם ליברה בע"מ מבקשת להודיע על החמרות ועדכונים בעלון לרופא של התכשיר שבנדון.

בהודעה זו מצוינים השינויים המהווים החמרה, מסומנים בקו תחתון. בעלון קיימים שינויים נוספים שאינם מהווים החמרה.

הרכב התכשירים- מרכיב פעיל:

Tramadol Hydrochloride 100mg/2ml

התוויה מאושרת:

Moderate to severe pain

צורת המתן:

Solution for Injection

ההחמרות בעלון לרופא נעשו בסעיפים הבאים:

Duration of administration

Tramal Injection 100 should under no circumstances be administered for longer than absolutely necessary. If long-term pain treatment with tramadol is necessary in view of the nature and severity of the illness, then careful and regular monitoring should be carried out (if necessary with breaks in treatment) to establish whether and to what extent further treatment is necessary.

4.3 Contraindications

Tramal Retard is contraindicated

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- in acute intoxication with alcohol, hypnotics, analgesics, opioids, or other psychotropic medicinal products;
- for use in narcotic withdrawal treatment.

4.4 Special warnings and precautions for use

- Tramadol 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 center or function, increased intracranial pressure.
- In patients sensitive to opiates tramadol should only be used with caution.
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- Concomitant use of tramadol and sedating medicinal products such as benzodiazepines or related substances, may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedating medicinal products should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe tramadol concomitantly with sedating medicinal products, the lowest effective dose of tramadol should be used, and the duration of the concomitant 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).

- 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.

- When a patient no longer requires therapy with tramadol, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal.

- **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.

- **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.

4.5 Interaction with other medicinal products and other forms of interaction

- The concomitant use of opioids with sedating medicinal products such as benzodiazepines or related substances increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect.
  The dose of tramadol and the duration of the concomitant use should be limited (see section 4.4)
- Tramadol can induce convulsions and increase the potential for selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, antipsychotics and other seizure threshold-lowering medicinal product (such as bupropion, mirtazapine, tetrahydrocannabinol) to cause convulsions.

- Concomitant therapeutic use of tramadol and serotonergic drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), MAO inhibitors (see section 4.3), tricyclic antidepressants and mirtazapine may cause serotonin toxicity…

4.6 Fertility, pregnancy and lactation

Pregnancy

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 should not be used in pregnant women.

Tramadol - administered before or during birth - does not affect uterine contractility. In neonates it may induce changes in the respiratory rate which are usually not clinically relevant. Chronic use during pregnancy may lead to neonatal withdrawal symptoms.

4.7 Undesirable effects

- *Vascular disorders:*

Uncommon: cardiovascular regulation (postural hypotension or cardiovascular collapse). These adverse reactions may occur especially on intravenous administration and in patients who are physically stressed.

- *Respiratory, thoracic and mediastinal disorders:*

Rare: respiratory depression, dyspnoea

If the recommended doses are considerably exceeded and other centrally depressant substances are administered concomitantly (see section 4.5), respiratory depression may occur.

Worsening of asthma has been reported, though a causal relationship has not been established.

- *Psychiatric disorders:*

Rare: hallucinations, confusion, sleep disturbance, delirium, anxiety and nightmares. Psychic adverse reactions may occur following administration of tramadol which vary individually in intensity and nature (depending on personality and duration of treatment). These include changes in mood (usually elation, occasionally dysphoria), changes in activity (usually suppression, occasionally increase) and changes in cognitive and sensorial capacity (e.g. decision behaviour, perception disorders). Drug dependence may occur.

- *Eye disorders:*

Rare: miosis, mydriasis, blurred vision

- *Gastrointestinal disorders:*

Uncommon: retching; gastrointestinal discomfort (a feeling of pressure in the stomach, bloating), diarrhea

- *Metabolism and nutrition disorders:*
  Not known: hypoglycaemia
- *General disorders*
  Common: fatigue

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