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רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

XXXX

Tramadol Medochemie 100mg/2ml

חברת דיפריס ושות' בע"מ מבקשת להודיע על עדכון העלון לרופא של התכשיר שבנדון.

ההתוויה הרשומה של התכשיר בישראל: Moderate to severe pain

צורת המתן של התכשיר : solution for injection/infusion

מרכיב פעיל: Tramadol hydrochloride 50mg/1ml

בהודעה זו מצוינים סעיפים בהם נעשה עדכון המהווה החמרה - מודגש בצהוב.
בעלון נעשו עדכונים נוספים על העדכונים המצויינים כאן.

עדכונים בעלון נעשו בסעיפים הבאים:

4.3 Contraindications

- 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.

Concomitant use of Tramadol Medochemie 100 mg/2 ml 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 Medochemie 100 mg/2 ml concomitantly with sedating medicinal products, the lowest effective dose of Tramadol Medochemie 100 mg/2 ml 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 situation.

Tolerance, psychic and physical dependence may develop, especially after long-term use.

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. Estimates of prevalence of ultra-rapid metabolisers in different populations are summarised below:

Population	Prevalence %
African/Ethiopian	29%
African American	3.4% to 6.5%
Asian	1.2% to 2%
Caucasian	3.6% to 6.5%
Greek	6.0%
Hungarian	6.0%
Northern European	1% to 2%

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 Medochemie 100 mg/2 ml 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 re-uptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, antipsychotics and other seizure threshold-lowering medicinal products (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. Serotonin syndrome is likely when one of the following is observed:

- Spontaneous clonus
- Inducible or ocular clonus with agitation or diaphoresis
- Tremor and hyperreflexia
- Hypertonia and body temperature > 38 °C and inducible or ocular clonus.
- Other active substances known to inhibit CYP3A4, such as ketoconazole and erythromycin, might inhibit the metabolism of tramadol (N-demethylation) probably also the metabolism of the active O-demethylated metabolite. The clinical importance of such an interaction has not been studied (see section 4.8).
- In a limited number of studies the pre- or postoperative application of the antiemetic 5-HT3 antagonist ondansetron increased the requirement of tramadol in patients with postoperative pain.

4.6 Effects on ability to drive and use machines

Even when taken according to instructions, tramadol may cause effects such as somnolence and dizziness and therefore may impair the reactions of drivers and machine operators. This applies particularly in conjunction with other psychotropic substances, particularly alcohol.

This medicine can impair cognitive function and can affect a patient's ability to drive safely.

4.7 Undesirable effects

Rapid intravenous administration may be associated with a higher incidence of adverse effects

and therefore should be avoided.

Cardiac disorders:

Uncommon: cardiovascular regulation (palpitation, tachycardia,). These adverse reactions may occur especially on intravenous administration and in patients who are physically stressed.

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

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

Nervous system disorders:

Common: headache, somnolence

Psychiatric disorders:

Rare: hallucinations, confusion, sleep disturbance, delirium, anxiety and nightmares.

Other symptoms that have very rarely been seen with tramadol discontinuation include: panic attacks, severe anxiety, hallucinations, …

Eye disorders

Rare: miosis, mydriasis, blurred vision

Gastrointestinal disorders:

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

Metabolism and nutrition disorders:

Not known: hypoglycaemia

General disorders: Common: fatigue

4.8 Overdose

Symptoms

… cardiovascular collapse,…

העלון מפורסם במאגר התרופות שבאתר משרד הבריאות:
https://data.health.gov.il/drugs/index.html#!/byDrug

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