Symol 100mg/2ml

(Tramadol HCl) Injection

سائمول 100 ملی گرام/2 ملی لیٹر

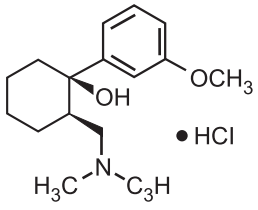
(ٹراماڈول ہائیڈروکلورائیڈ) انجکشن

COMPOSITION

Each 2ml ampoule contains:
Tramadol .....100mg.
(As Tramadol HCl USP)
Finished Product Specs.: In-house.

DESCRIPTION

Symol (Tramadol HCl) is a centrally acting opioid analgesic. It also has noradrenergic and serotonergic properties that may contribute to its analgesic activity. Chemically, it is (±)-cis-2-[(Dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol hydrochloride. Its molecular formula is $C_{16}H_{25}NO_2$.HCl and the structural formula is:



(Tramadol HCl)

CLINICAL PHARMACOLOGY

Mechanism of Action

Tramadol is a centrally acting analgesic which possesses opioid agonist properties. Tramadol consists of two enantiomers, the (+)-isomer is predominantly active as an opioid with preferential activity for the μ-receptor. The (-)- isomer potentiates the analgesic effect of the (+)-isomer and is active as an inhibitor of noradrenaline and serotonin uptake, thereby modifying the transmission of pain impulses.

Pharmacokinetics

Absorption

More than 90% of Tramadol is absorbed after oral administration. The mean absolute bioavailability is approximately 70%, irrespective of the concomitant intake of food.

Distribution

The distribution of tramadol after an intravenous administration is rapid and is biphasic with different half-lives of 0.31 ± 0.17 hours which is the initial rapid phase and 1.7 ± 0.4 hours which is the slower phase respectively. After intravenous administration of 100mg tramadol, the serum concentration was 613 ± 221ng/ml at 15 minutes post dosing and 409 ± 79ng/ml at 2 hours post dosing.

Metabolism

Tramadol undergoes hepatic metabolism with approximately 85% of an oral and intravenous dose. Tramadol is metabolised by N and O-desmethylation via the cytochrome P450 iso enzymes CYP3A4 and CYP2D6 and glucuronidation or sulfation in the liver. The metabolite O-desmethyltramadol is pharmacologically active.

Elimination:

Tramadol is essentially excreted via the kidneys. The mean elimination half-life of tramadol following oral and intravenous administration is 5 - 6 hours. Approximately 90% of an oral dose is excreted by the kidneys. Total clearance of tramadol was 28.0L/h following intravenous administration.

Special Population:

Effect of age

In elderly patients aged over 75 years, the terminal elimination half- life was 7.0 ± 1.6 hours compared to 6.0 ± 1.5 hours in adults after oral administration.

Hepatic or Renal impairment

The terminal half-life of elimination ($t_{1/2}$) of tramadol may be prolonged in patients with hepatic or renal dysfunction. In liver cirrhosis patients, the mean $t_{1/2}$ of tramadol was 13.3 ± 4.9 hours. In patients with renal failure (creatinine clearance < 5ml/min) the $t_{1/2}$ of tramadol was 11.0 ± 3.2 hours and that of O-desmethyltramadol was 16.9 ± 3.0 hours .

THERAPEUTIC INDICATIONS

For the treatment and prevention of moderate to severe pain.

POSOLOGY AND METHOD OF ADMINISTRATION

Tramadol 50mg/ml Solution for Injection should not be administered for longer than absolutely necessary. If long-term pain treatment with Tramadol 50mg/ml Solution for Injection is necessary in view of the nature and severity of the illness, then careful regular monitoring should be carried out (if necessary with breaks in treatment) to establish whether and to what extent, further treatment is necessary.

The dose should be adjusted according to the intensity of the pain and the sensitivity of the individual patient. The lowest effective dose for analgesia should generally be selected.

Special Precautions:

The total daily dose of 400mg tramadol hydrochloride should not be exceeded, except in special clinical circumstances.

Adults and children 12 years and over

The usual dose is 50mg 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.

Special Population:

Geriatric patients

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.

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.

ADVERSE REACTIONS

Very common: Dizziness, vomiting and nausea.
Common: Headache, drowsiness, constipation, dry mouth, sweating and fatigue.
Uncommon: Effects on cardiovascular regulation (palpitation, tachycardia, postural hypotension or cardiovascular collapse), retching, gastrointestinal irritation (a feeling of pressure in the stomach, bloating) and dermal reactions (e.g. pruritus, rash, urticaria).

CONTRAINDICATION

Tramadol HCl is contraindicated in:

- Patients with known hypersensitivity to tramadol HCl or to any excipient of the product.
- Patients suffering from acute intoxication with hypnotics, centrally acting analgesics,opioids,psychotropic drugs or alcohol.
- Patients who are receiving monoamine oxidase (MAO) inhibitors or who have taken them within the last 14 days.
- Patients suffering from uncontrolled epilepsy.
  Narcotic withdrawal treatment.

PRECAUTIONS

- Tramadol has a low dependence potential. On long-term use tolerance, psychic and physical dependence may develop. Convulsions have been reported at therapeutic doses and the risk may be increased at doses exceeding the usual upper daily dose limit.
- Tramadol HCl should be used with prudence in patients who have shown previous hypersensitivity to opiates and in patients with severe renal or hepatic impairment, head injury, decreased level of consciousness, increased intracranial pressure, or patients in shock or at risk of convulsions.
- In patients sensitive to opiates, tramadol HCl should only be used with caution.
- Care should be taken when administering tramadol HCl to patients with existing respiratory depression or excessive bronchial secretion and in those patients taking concomitant CNS depressant drugs.

Pregnancy

There is inadequate evidence available on the safety of tramadol HCl in human pregnancy. Therefore, it should not be used in pregnant women.

Nursing Mothers

Tramadol HCl should not be administered during breast feeding as tramadol and its metabolites have been detected in breast milk. 0.1% of the dose administered to the mother may be excreted in milk.

DRUG INTERACTIONS

- Tramadol may potentiate the CNS depressant effects of other centrally acting drugs (including alcohol) when administered concomitantly with such drugs.
- Tramadol can induce convulsions and increase the potential for selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, anti-psychotics and other seizure threshold lowering medicinal products (such as bupropion, mirtazapine, tetrahydrocannabinol) to cause convulsions.
- Administration of tramadol HCl together with carbamazepine results in markedly decreased serum concentrations of tramadol which may reduce analgesic effectiveness and shorten the duration of action.
- Caution should be exercised during concomitant treatment with tramadol and coumarin derivatives (e.g. warfarin) due to increased INR and ecchymoses in some patients.
- Tramadol for Injection should not be combined with MAO inhibitors.

OVERDOSAGE

Symptoms

Symptoms of tramadol overdose include vomiting, miosis, sedation, seizures, respiratory depression and hypotension,with circulatory failure and coma. Respiratory failure may also occur. Such symptoms are typical of opioid analgesics.

Treatment

Treatment of overdose requires the maintenance of the airway and cardiovascular functions. Respiratory depression may be reversed using naloxone and fits controlled with diazepam. The treatment of acute overdose of tramadol using hemodialysis or hemofiltration alone is not sufficient or suitable due to the slow elimination of tramadol from the serum by these routes.

STORAGE

- Store below 30°C.
- Protect from heat and light.

PRESENTATION

Symol (Tramadol HCl) Injection 100mg/2ml are available in pack of 5's.

To be sold on the prescription of a registered medical practitioner only.

Keep all medicines out of the reach of children

Manufactured by:
Indus Pharma (Pvt.) Ltd.
65/27, Korangi Industrial Area,
Karachi-74900, Pakistan.

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