LEAF INSERT

TRAMSARAN INJECTION 100mg/2ml
(TRAMADOL HYDROCHLORIDE USP)

LABEL CLAIM:
Each 2ml contains :
Tramadol hydrochloride BP…….100mg
Innovator's Specs.

QUALITATIVE AND QUANTITATIVE COMPOSITION

- Tramadol hydrochloride
- Sodium Acetate Trihydrate
- Hydrochloric acid
- Sodium Hydroxide
- Water for Injection

EXCIPIENTS WITH KNOWN EFFECTS:
None

PHARMACEUTICAL FORM

Solution for intramuscular injection or concentrate for solution for infusion.

CLINICAL DATA:

THERAPEUTIC INDICATIONS:

Tramsaran 100mg Injection is used for the treatment and prevention of moderate to severe pain..

DOSAGE AND ADMINISTRATION:

Tramsaran 100mg Injection should not be administered for longer than absolutely necessary. If long-term pain treatment with Tramsaran 100mg 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 lowest effective dose for analgesia should generally be selected. The Tramadol HCl solution is for parenteral injection either intramuscularly, by slow intravenous injection or diluted in solution for administration by infusion or patient controlled analgesia.

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.

Geriatric patients: A dose adjustment is not usually necessary in patients up to 75 years without clinically manifest hepatic or renal insufficiency.

Renal insufficiency/dialysis and hepatic impairment: In patients with renal and/or hepatic insufficiency the elimination of Tramadol HCl 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.

Method of administration

Parenteral

CONTRA-INDICATIONS:

Tramsaran 100mg Injection should not be given to patients who have previously demonstrated hypersensitivity towards Tramadol HCl or any of the other ingredients. Tramsaran 100mg Injection should not be given to patients suffering from acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids or psychotropic drugs. Tramadol HCl should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal. Tramsaran 100mg Injection is contraindicated in patients with epilepsy not adequately controlled by treatment. Tramadol HCl must not be used in narcotic withdrawal treatment.

WARNING & PRECAUTION FOR USE:

Concomitant use of Tramsaran 100mg Injection and sedating medicinal substances such as benzodiazepines or related substances, may result in respiratory depression, sedation, coma and death. Concomitant prescribing with these sedating medicinal products should be only undertaken where no other option is available. If concomitant prescribing is the only option, the lowest effective dose of Tramadol HCl should be used, and duration of concomitant treatment should be as short as possible. Patients should be monitored closely for signs and symptoms of respiratory depression and sedation. It is recommended to inform patients and their caregivers to be aware of these symptoms.

Post-operative use in children: Extreme caution should be exercised when Tramadol HCl 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 HCl 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. In patients sensitive to opiates the product should only be used with caution. Patients with a history of epilepsy or those susceptible to seizures should only be treated with Tramadol HCl if there are compelling reasons. The risk of convulsions may increase in patients taking. Care should be taken when treating patients with respiratory depression, or if concomitant CNS depressant drugs are being administered, or if the recommended dosage is significantly exceeded, as the possibility of respiratory depression cannot be excluded in these situations. At therapeutic doses respiratory depression has infrequently been reported. Tramadol HCl administration during anaesthesia comprising continuous administration of isoflurane have shown clinically significant lightening of anaesthetic depth or intra-operative recall. Therefore providing the current practice of administering continuous, potent (volatile or intravenous) anaesthetic agent is followed; Tramadol HCl may be used intra- operatively in the same way as other analgesic agents are routinely used.

DRUG INTERACTIONS:

Tramsaran 100mg Injection should not be combined with MAO inhibitors. In patients treated with MAO inhibitors in the 14 days prior to the use of the opioid pethidine, lifethreatening interactions on the central nervous system, respiratory and cardiovascular function have been observed. 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. Concomitant administration of Tramsaran 100mg Injection with other centrally acting drugs, including alcohol, may potentiate CNS depressant effects. 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 products (such as bupropion, mirtazapine, tetrahydrocannabinol) to cause convulsions. Theoretically there is a possibility that tramadol could interact with lithium. Concomitant therapeutic use of tramadol and serotonergic drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), MAO inhibitors, tricyclic antidepressants and mirtazapine may cause serotonin toxicity. There have been isolated reports of interaction with coumarin anticoagulants resulting in an increased INR with major bleeding and ecchymoses in some patients and so care should be taken when commencing treatment with Tramadol HCl in patients on anticoagulants. The simultaneous administration of carbamazepine markedly decreases serum concentrations of Tramadol HCl to an extent that a decrease in analgesic effectiveness and a shorter duration of action may occur. With the concomitant or previous administration of cimetidine clinically relevant interactions are unlikely to occur. Therefore no alteration of the tramadol dosage regimen is recommended for patients receiving chronic cimetidine therapy. Other active substances known to inhibit CYP3A4, such as ketoconazole and erythromycin, might inhibit the metabolism of Tramadol HCl (N-demethylation) probably also the metabolism of the active O-demethylated metabolite. The pre- or postoperative application of the antiemetic 5-HT3 antagonist ondansetron increased the requirement of Tramadol HCl in patients with postoperative pain.

REPRODUCTION, PREGNANCY AND BREAST-FEEDING:

Pregnancy:
There is inadequate evidence available on the safety of Tramadol HCl in human pregnancy, therefore Tramsaran 100mg Injection should not be used in pregnant women.

Breast-feeding:
Approximately 0.1% of the maternal dose of Tramadol HCl is excreted in breast milk. For this reason Tramsaran 100mg Injection should not be administered during breast-feeding or alternatively, breast-feeding should be discontinued during treatment with Tramadol HCl.

Fertility:
Post marketing surveillance does not suggest an effect of tramadol on fertility.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

Patients who experience visual disturbances, dizziness, vertigo, somnolence, central nervous system disturbances, drowsiness or fatigue while taking NSAIDs should refrain from driving or operating machinery.

UNDESIRABLE EFFECTS:

Cardiovascular system disorders:
Cardiovascular regulation (palpitation, tachycardia, postural hypotension or cardiovascular collapse). These adverse effects may occur especially after intravenous administration and in patients.
Nervous system disorders:
Dizziness, headache, somnolence, changes in appetite, paraesthesia, tremor, epileptiform convulsions, involuntary muscle contractions and abnormal coordination, syncope and speech disorders. Epileptiform convulsions occurred mainly after administration of high doses of Tramadol HCl or after concomitant treatment with medicinal products which can lower the seizure threshold.
Psychiatric disorders:
Hallucinations, confusion, sleep disturbance, delirium, anxiety and nightmares. Psychic side effects may occur following administration of tramadol, which vary individually in intensity and nature (depending on personality and duration of medication). These include changes in mood (usually elation, occasionally dysphoria), changes in activity (usually suppression, occasionally increase) and changes in cognitive and sensorial ability (e.g. decision behaviour, perception disorders). Dependence may occur.
Eye disorders:
Blurred vision, miosis and mydriasis.
Respiratory system disorders:
Respiratory depression and dyspnoea. If the recommended doses are considerably exceeded and other centrally depressant substances are administered concomitantly, respiratory depression may occur. Worsening of asthma has been reported, though a causal relationship has not been established.
Gastrointestinal disorders:
Nausea, vomiting, constipation, dry mouth, retching, gastrointestinal irritation (a feeling of pressure in the stomach, bloating) and diarrhoea
Skin and subcutaneous disorders:
Sweating and dermal reactions (e.g. pruritus, rash, urticaria).
Musculo-skeletal system disorders:
Muscle weakness.
Hepatobiliary system disorders:
In a few isolated cases, increases in liver enzyme values have been reported in a Tramadol HCl connection with the therapeutic use of tramadol.
Renal and urinary system disorders: Micturition disorders (difficulty in passing urine, dysuria and urinary retention)
General disorders: Fatigue.
Immune system disorders: Allergic reactions (e.g. dyspnoea, bronchospasm, wheezing, angioneurotic oedema) and anaphylaxis.
Metabolism and nutrition disorders: Changes in appetite.

OVERDOSE

Symptoms

There is no typical clinical picture resulting from diclofenac over dosage. Over dosage can cause symptoms such as vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible.

Therapeutic measures

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adult's gastric lavage should be considered within one hour of ingestion of potentially toxic amounts. Frequent or prolonged

convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition.

PHARMACOLOGICAL PROPERTIES:

Pharmacodynamic properties (with Pharmacotherapeutic class):

Pharmacotherapeutic group

Pharmacotherapeutic category: non-steroidal antinflammatory drugs (NSAIDs):

ATC Code: M01AB05.

It is therapeutic subgroup classification: musculo-skeletal system/anti-inflammatory and antirheumatic products/ non-steroids/acetic acid derivatives and related substances

Mechanism of action:
Tramadol HCl is a centrally acting synthetic opioid analgesic and SNRI (serotonin/norepinephrine reuptake-inhibitor) that is structurally related to and Due to its good tolerability profile and multimodal mechanism of action, Tramadol HCl is generally considered a lower-risk opioid option for the treatment of moderate to severe pain.

PHARMACOKINETICS:

Absorption & Distribution:
More than 90% of Tramadol HCl is absorbed after oral administration. The mean absolute bioavailability is approximately 70%, irrespective of the concomitant intake of food. The difference between absorbed and non-metabolised available Tramadol HCl is probably due to the low first-pass effect. The first-pass effect after oral administration is a maximum of 30%. Tramadol HCl has a plasma protein binding of about 20%. It passes the blood-brain and placental barriers. Very small amounts of the substance and its O-desmethyl derivative are found in the breast-milk (0.1% and 0.02% respectively of the applied dose).

Metabolism & Elimination:
In humans Tramadol HCl is mainly metabolised by means of N- and O-demethylation and conjugation of the O-demethylation products with glucuronic acid. Only O-desmethyltramadol HCl is pharmacologically active. Tramadol HCl and its metabolites are almost completely excreted via the kidneys. Cumulative urinary excretion is 90% of the total radioactivity of the administered dose. In cases of impaired hepatic and renal function the half-life may be slightly prolonged. Elimination half-life t1/2,ß is approximately 6 h, irrespective of the mode of administration. In patients above 75 years of age it may be prolonged by a factor of approximately 1.4.

Paediatric population:
The pharmacokinetics of Tramadol HCl and O-desmethyltramadol after single-dose and multiple- dose oral administration to subjects aged 1 year to 16 years were found to be generally similar to those in adults when adjusting for dose by body weight, but with a higher between-subject variability in children aged 8 years and below.

PHARMACEUTICAL DATA:

Store below 30ºC.
Protect from heat and light.
Keep out of the reach of children.

PRESENTATION:

Tramsaran 100mg Injection is available in pack size of 2ml x 5’s

MEDICINE ON PRESCRIPTION ONLY:

List 1

MARKETING AUTHORIZATION HOLDER:

SARAN PHARMA
ABIDJAN COCODY 2 PLATEAUX DERRIERE L’EN, RUE J5, LOT 269, SECTION KX PARCELLE 104, 08 BP 3121 ABIDJAN 08 RCI

MANUFACTURED BY:

Surge Laboratories (Pvt.) Ltd.
10th Km, Faisalabad Road, Bikhi
District, Sheikhupura-Pakistan.

DATE OF LAST REVISION:

November 2024