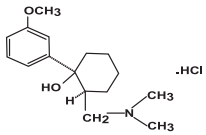
Tonoflex®

SR 100mg Tablets / 50mg Capsules / 100mg/2ml Injection

(Tramadol HCl)

DESCRIPTION:
Tramadol hydrochloride is a centrally acting analgesic. The chemical name for tramadol hydrochloride is (±)cis-2-[(Dimethylamino)methyl]-1-(3-Methoxyphenyl) cyclohexanol hydrochloride. Its structural formula is:



COMPOSITION:
***Tonoflex*® SR 100mg Tablets**
Each film coated tablet contains: Tramadol HCl Ph. Eur.....100mg

***Tonoflex*® 50mg Capsules**
Each capsule contains: Tramadol HCl Ph. Eur..... 50mg

***Tonoflex*® 100mg/2ml Injection**
Each 2ml ampoule contains: Tramadol HCl Ph. Eur..... 100mg

INDICATIONS:
Tramadol hydrochloride is indicated for the management of moderate to moderately severe chronic pain

PHARMACODYNAMICS:
Tramadol hydrochloride is a centrally acting synthetic opioid analgesic. Two mechanisms of action appear applicable, binding of parent and M1 metabolite to μ-opioid receptors and weak inhibition of reuptake of nor-epinephrine and serotonin. Analgesia in humans begins approximately within one hour after administration and reaches a peak after two to three hours

PHARMACOKINETICS:
Absorption
Tramadol hydrochloride is rapidly and almost completely absorbed after oral administration. Food does not significantly affect its rate or extent of absorption, therefore, tramadol hydrochloride can be administered without regard to food. After intramuscular administration in humans, tramadol is absorbed rapidly and completely; the mean peak serum concentration (C_{max}) is reached after 45 minutes and bioavailability is almost 100%

Distribution
Tramadol has high tissue affinity. The volume of distribution of tramadol was 2.6 and 2.9 liters/kg in the male and female subjects, respectively, following a 100mg intravenous dose. The binding of tramadol hydrochloride to human plasma proteins is approximately 20%

Metabolism
Tramadol hydrochloride is extensively metabolized after oral administration. Approximately 30% of the dose is excreted in the urine as unchanged drug, whereas 60% of the dose is excreted as metabolites. The major metabolic pathways appear to be N- and O-demethylation and glucuronidation or sulfation in the liver

Elimination
Tramadol hydrochloride is eliminated primarily through metabolism by the liver and the metabolites are eliminated primarily by the kidneys

DOSAGE AND ADMINISTRATION:
Tramadol hydrochloride is given by mouth, intramuscular, subcutaneous, or intravenous route. Usual doses by mouth are 50 to 100mg every 4 to 6 hours. The total daily dosage by mouth should not exceed 400mg/day
A dose of 50 to 100mg may be given every 4 to 6 hours by intramuscular, intravenous injection over 2 to 3 minutes, or by the intravenous infusion. For the treatment of post operative pain, the initial dose is 100mg followed by 50mg every 10 to 20 minutes if necessary to a total maximum (Including the initial dose) of 250mg in the first hour. Thereafter, doses are 50 to 100mg every 4 to 6 hours up to a total daily dose of 600mg

OR
As directed by the physician

CONTRA-INDICATIONS:
Tramadol hydrochloride is not recommended for the following groups:
- Patients with known hypersensitivity to tramadol hydrochloride or opioids
- Patients with acute intoxication of alcohol, hypnotics, narcotics, centrally acting analgesics, opioids or psychotropic drugs

Tramadol hydrochloride should not be used in patients with:
Creatinine clearance less than 30ml/min, or severe hepatic impairment (Child-Pugh class C)

DRUG INTERACTION:
CYP2D6 and CYP3A4 inhibitors
Concomitant administration of CYP2D6 and / or CYP3A4 inhibitors, such as quinidine, fluoxetine, paroxetine and amitriptyline (CYP2D6 inhibitors), and ketoconazole and erythromycin (CYP3A4 inhibitors), may reduce metabolic clearance of tramadol increasing the risk for serious adverse events including seizures and serotonin syndrome
Caution is advised when tramadol hydrochloride is co-administered with other drugs that may affect the serotonergic neurotransmitter systems, such as SSRIs, MAOIs, triptans, linezolid, lithium
Patients taking carbamazepine, a CYP3A4 inducer, may have a significantly reduced analgesic effect of tramadol hydrochloride

WARNINGS AND PRECAUTIONS:
Seizure Risk
Seizures have been reported in patients receiving tramadol hydrochloride within the recommended dosage range

Concomitant use of tramadol hydrochloride increases the seizure risk in patients taking
Selective serotonin re-uptake inhibitors (SSRI antidepressants or anorectics)
Tricyclic antidepressants (TCAs), and other tricyclic compounds (e.g. Cyclobenzaprine, promethazine etc.), or other opioids

Administration of tramadol hydrochloride may enhance the seizure risk in patients taking

180mm

150mm

MAO inhibitors, neuroleptics, and other drugs that reduce the seizure threshold. Risk of convulsions may also increase in patients with epilepsy, those with a history of seizures, or in patients with a recognized risk for seizure

Suicide Risk
Do not prescribe tramadol hydrochloride for patients who are suicidal or addiction-prone
Caution must be taken if prescribing tramadol hydrochloride for patients taking tranquilizers or antidepressant drugs and patients who use alcohol in excess

Tell your patients not to exceed the recommended dose and to limit their intake of alcohol

Serotonin Syndrome Risk
The development of a potentially life-threatening serotonin syndrome may occur with use of tramadol hydrochloride products, tramadol hydrochloride products in excessive doses, either alone or in combination with other CNS depressants, including alcohol, are a major cause of drug-related deaths

Anaphylactoid Reactions
Serious and rarely fatal anaphylactoid reactions have been reported in patients receiving therapy with tramadol. When these events do occur it is often following the first dose

Respiratory Depression
Administer tramadol cautiously in patients at risk for respiratory depression

Use in Ambulatory Patients
Tramadol hydrochloride may impair the mental and / or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using this drug should be cautioned accordingly

Withdrawal
Withdrawal symptoms may occur if tramadol hydrochloride is discontinued abruptly. These symptoms may include: Anxiety, sweating, insomnia, rigors, pain, nausea, tremors, diarrhoea, upper respiratory symptoms, piloerection, and rarely hallucinations

Drug Abuse And Addiction
Tramadol hydrochloride is a μ-agonist opioid. Tramadol hydrochloride, like other opioids used in analgesia, can be abused and is subject to criminal diversion. Drug addiction is characterized by compulsive use, use for non-medical purposes, and continued use despite harm or risk of harm. Drug addiction is a treatable disease, utilizing a multi-disciplinary approach, but relapse is common

PREGNANCY:
There are no adequate and well-controlled studies in pregnant women

Pregnancy Rick Category C: There is inadequate evidence available on the safety of tramadol in human pregnancy. Therefore, tramadol should not be used in pregnancy

Labor and Delivery
Tramadol hydrochloride should not be used in pregnant women prior to or during labor unless the potential benefits outweigh the risks. When given before or during birth, tramadol does not affect uterine contractility. In neonates it may induce changes in respiratory rate, which are usually clinically not relevant

Nursing Mothers
Tramadol hydrochloride is not recommended for post delivery analgesia in nursing mothers because small quantities (About 1% of the maternal dose) is secreted into breast milk. Therefore, tramadol should not be used during lactation. After single administration of tramadol, it is not usually necessary to interrupt breast feeding

Paediatric Use
The safety and efficacy of tramadol hydrochloride in patients under 16 years of age have not been established. The use of tramadol hydrochloride in the paediatric population is therefore not recommended

Geriatric Use
In general, higher incidence rates of adverse events were observed for patients older than 65 years of age. For this reason, tramadol hydrochloride should be used with great caution in patients older than 75 years of age

SIDE-EFFECTS:
Malaise, anxiety, confusion, euphoria, miosis, nervousness, sleep disorders, abdominal pain, anorexia, flatulence and rash

OVER DOSAGE:
Serious potential consequences of over dosage are respiratory depression, lethargy, coma, seizure, cardiac arrest and death. Primary attention should be given to maintaining adequate ventilation along with general supportive treatment. Naloxone can reverse some, but not all, symptoms caused by the over dosage. Hemodialysis is not expected to be helpful in an overdose because it removes less than 7% of the administered dose in a 4-hours dialysis period

STABILITY:
See expiry on the pack

PRESENTATION:
Tonoflex® SR 100mg tablets in a pack of 10's
Tonoflex® 50mg capsules in a pack of 10's
Tonoflex® 100mg/2ml injection in a pack of 5's

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light, humidity and freezing
Store between 15 to 30°C
Improper storage may deteriorate the medicine
Caution: Injection should not be used if container is leaking, solution is cloudy or it contains un-dissolved particle(s)

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

ٹونوفلیکس ایس آر ۱۰۰ ملی گرام ٹیبلٹ / ۵۰ ملی گرام کیپسول / ۱۰۰ ملی گرام / ۲ ملی لیٹر انجکشن

(ٹراماڈال ہائیڈروکلورائیڈ)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ہدایات: بچوں کی پہنچ سے دور رکھیں

دوا کو دھوپ، گرمی، نمی اور منجمد ہونے سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ

کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

تنبیہ: انجکشن کے لیک ہونے، دُھندلا ہونے یا اس میں کوئی غیر حل پذیر شے

نظر آنے کی صورت میں ہرگز استعمال نہ کریں

P002070/S

R.N-04/HA/04/16/Inj.

180mm

150mm