

120mm

Tonoflex^{®-P} Tablets (Tramadol HCl + Paracetamol)

COMPOSITION:

Each film coated tablet contains:
Tramadol HCl Ph. Eur..... 37.5mg
Paracetamol BP.....325mg

CLINICAL PHARMACOLOGY:

Mode of Action

Tramadol is a centrally acting synthetic analgesic compound whose analgesic profile can be attributed to the binding of parent and O-demethylated (M1) metabolite to μ -opioid receptors as well as the weak inhibition of neuronal re-uptake of noradrenaline and serotonin. Paracetamol also has centrally acting analgesic effects

PHARMACOKINETICS:

Tramadol is well absorbed after oral administration, reaching peak activity in 2 to 3 hours. Oral absorption of paracetamol following co-administration of tramadol and paracetamol, gives a peak plasma concentration of paracetamol within one hour and is not affected by co-administration with tramadol. Tramadol and paracetamol are both extensively metabolised in the liver. Approximately 30% of tramadol is excreted unchanged in the urine. Tramadol and its metabolites are eliminated primarily by the kidney. The plasma elimination half-lives of tramadol and its M1 metabolite are approximately 6 and 7 hours respectively. Paracetamol is eliminated from the body primarily by formation of glucuronide and sulfate conjugates in a dose-dependent manner. The half-life of paracetamol is about 2-3 hours in adults. Less than 9% of paracetamol is excreted unchanged in the urine

INDICATIONS:

Tonoflex^{®-P} tablets are indicated for the short term (Less than 5 days) management of acute pain

CONTRAINDICATIONS:

Tramadol + Paracetamol combination is contraindicated in patients with a known hypersensitivity to tramadol, paracetamol or other opioids such as codeine. It is also contraindicated in cases of severe liver function impairment and in acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids or psychotropic medicines. It should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal. Tramadol + Paracetamol combination must not be used for narcotic withdrawal treatment. Tramadol + Paracetamol combination should not be given to patients with respiratory depression especially in the presence of cyanosis and excessive bronchial secretions. Tramadol + Paracetamol combination should not be given to patients with increased intracranial pressure or central nervous system depression due to head injury or cerebral disease

WARNINGS:

Dosages in excess of those recommended may cause severe liver damage. Patients suffering from liver or kidney disease should take paracetamol containing products under medical supervision

Serious Skin Reactions

Rarely, acetaminophen (paracetamol) may cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Patients should be informed about the signs of serious skin reactions, and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity

Seizures

Seizures have been reported in patients receiving tramadol at dosages within the recommended dosage range. The risk of seizures is enhanced in patients exceeding the recommended dose, or in patients taking tricyclic anti-depressants or other tricyclic compounds e.g. promethazine, selective serotonin re-uptake inhibitors, MAO-inhibitors and neuroleptics

Drug Abuse and Dependence

Although tramadol has a low dependence potential, tolerance, psychic and physical dependence of the morphine-type (μ Opioid) may develop with long-term use

Effects on Ability to Drive or Operate Machinery

Tramadol may affect reactions to the extent that driving ability and the ability to operate machinery may be impaired. This applies particularly in conjunction with other psychotropic medicines including alcohol

DOSAGE AND ADMINISTRATION:

To be used in adults and children over 16 years of age. Do not exceed the recommended dose

Acute Pain

2 tablets every 4 to 6 hours as needed for pain relief. Do not exceed 8 tablets per day

Renal Impairment

In patients with creatinine clearance less than 30ml/min, it is recommended that the dosing interval be increased not to exceed 2 tablets every 12 hours

OR

As directed by the physician

SIDE-EFFECTS:

The most frequently reported side effects were of the gastrointestinal and central nervous systems. These include:

Gastrointestinal System

Nausea, abdominal pain, constipation, flatulence, vomiting, dry mouth, dyspepsia and diarrhoea

Central Nervous System and Psychiatric

Dizziness, headache, nervousness, anxiety, agitation, euphoria, emotional lability, hallucinations, hypertonia and tremor. Somnolence, insomnia, anorexia, anxiety, confusion, euphoria and nervousness

Other reported side-effects include pruritus, fatigue, upper respiratory tract infection, increased sweating, hot flushes, rashes and asthenia

Other side-effects reported with the use of tramadol include: anaphylaxis, increased liver enzyme values, postural hypotension or cardiovascular collapse and the potential for Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome

Paracetamol may cause allergic reactions and skin rash. The rash usually appears as red areas or allergic wheals, and may be accompanied by fever and involvement of the mucous membranes. The use of paracetamol has been associated with the occurrence of neutropenia, pancytopenia and leucopenia

210mm

PRECAUTIONS:**Pregnancy****Teratogenic Effects:** Pregnancy Category C

Safety during pregnancy and lactation has not been established, Tramadol has been shown to cross the placenta

Children

Safety and efficacy have not been established

Elderly

Use with caution, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease and multiple drug therapy

SPECIAL PRECAUTIONS:Do not co-administer **Tonoflex-P** with other tramadol or paracetamol containing products. Tramadol + Paracetamol combination should not be taken with alcohol containing beverages. The administration of tramadol + paracetamol combination concurrently with central nervous system (CNS) depressants such as alcohol, opioids, anaesthetic agents, phenothiazines, tranquilizers or sedative hypnotics is likely to intensify and prolong CNS effects

Tramadol + Paracetamol combination should be used with caution in patients with impaired renal functions, in patients with impaired hepatic functions and in patients prone to convulsive disorders or in shock

DRUG INTERACTIONS:

Concomitant administration of tramadol + paracetamol combination and carbamazepine may cause significantly decreased tramadol and M1 concentrations. Patients receiving carbamazepine may have significantly reduced analgesic effect from the tramadol component of tramadol + paracetamol combination. Concomitant administration with inhibitors of CYP2D6 such as fluoxetine, paroxetine, quinidine and amitriptyline could result in some inhibition of the metabolism of tramadol. Simultaneous administration with cimetidine is associated with clinically insignificant changes in serum concentrations of tramadol. Therefore, no alteration of the tramadol + paracetamol dosage regimen is recommended for patients receiving chronic cimetidine therapy

Tramadol + Paracetamol combination must not be combined with a MAO-inhibitor, or within 14 days of discontinuation of it, as potentiation of serotonergic and noradrenergic effects may result

Periodic evaluation of prothrombin time should be performed when tramadol + paracetamol is administered concurrently with warfarin like compounds

Concomitant administration of diflunisal and paracetamol produces a 50% increase in paracetamol plasma levels in normal volunteers.

Tramadol + Paracetamol combination should be used cautiously and patients should be monitored carefully

PRESENTATION:**Tonoflex-P** tablets in a pack of 10's**STABILITY:**

See expiry on the pack

INSTRUCTIONS:

Keep out of reach of children

Avoid exposure to heat, light and humidity

Store between 15 to 30°C

Improper storage may deteriorate the medicine

ٹونوفلیکس-پی ٹیبلٹ

(ٹراماڈال ہائیڈروکلورائیڈ + پیراسیٹامول)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ہدایات: بچوں کی پہنچ سے دور رکھیں

دوا کو دھوپ، گرمی اور نمی سے محفوظ رکھیں۔ اسے ۳۰ ڈگری سینٹی گریڈ

کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
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