TRAMACEL-P

Acetaminophen and Tramadol Hydrochloride Tablets USP

Composition:

Each film coated tablet contains:

Acetaminophen USP	325 mg
Tramadol Hydrochloride USP	37.5 mg
Excipients	q.s.

Colour : Sunset Yellow Lake

DESCRIPTION:

Acetaminophen and Tramadol Hydrochloride Tablets USP is indicated for the symptomatic treatment of moderate to severe pain. Acetaminophen and Tramadol Hydrochloride Tablets USP is an orange coloured, elongated, biconvex film coated tablets having score line on one side & plain on the other side.

INDICATION:

Acetaminophen and Tramadol Hydrochloride Tablets USP are indicated for the symptomatic treatment of moderate to severe pain.

The use of Acetaminophen and Tramadol Hydrochloride Tablets USP should be restricted to patients whose moderate to severe pain is considered to require a combination of Tramadol and Acetaminophen.

PHARMACOKINETIC:

Tramadol is administered in racemic form and the [-] and [+] forms of tramadol and its metabolite M1, are detected in the blood. After a single oral administration of a tramadol/Acetaminophen (37,5 mg/325 mg) tablet, peak plasma concentrations of 64.3/55.5 ng/ml [(+)-tramadol/(-)-tramadol] and 4.2 µg/ml (Acetaminophen) are reached after 1.8 h [(+)-tramadol/(-)-tramadol] and 0.9 h (Acetaminophen) respectively. The mean elimination half-lives t1/2 are 5.1/4.7 h [(+)-tramadol/(-)-tramadol] and 2,5 h (Acetaminophen).

Absorption:

Racemic tramadol is rapidly and almost completely absorbed after oral administration. The mean absolute bioavailability of a single 100 mg dose is approximately 75 %.

After administration of Acetaminophen and Tramadol Hydrochloride Tablets USP , the oral absorption of Acetaminophen is rapid and nearly complete and takes place mainly in the small intestine.

Distribution:

Tramadol has a high tissue affinity (Vd_{ss}=203 ± 40 l). It has a plasma protein binding of about 20%.

Acetaminophen appears to be widely distributed throughout most body tissues except fat. Its apparent volume of distribution is about 0.9 l/kg.

Metabolism:

Tramadol is extensively metabolized after oral administration. About 30 % of the dose is excreted in urine as unchanged drug, whereas 60% of the dose is excreted as metabolites.

Acetaminophen is principally metabolized in the liver through two major hepatic routes: glucuronidation and sulphation. The latter route can be rapidly saturated at doses above the therapeutic doses.

Elimination:

Tramadol and its metabolites are eliminated mainly by the kidneys. The half-life of Acetaminophen is approximately 2 to 3 hours in adults. It is shorter in children and slightly longer in the newborn and in cirrhotic patients. In renal insufficiency, the half-life of both compounds is prolonged.

PHARMACODYNAMIC:

Pharmacotherapeutic group: Tramadol, combinations

ATC code: N02AX 52

ANALGESICS

Tramadol is an opioid analgesic that acts on the central nervous system. Tramadol is a pure non selective agonists of the µ, δ, and κ opioid receptors with a higher affinity for the µ receptors. Other mechanisms which contribute to its analgesic effect are inhibition of neuronal reuptake of noradrenaline and enhancement of serotonin release. Tramadol has an antitussive effect. Unlike morphine, a broad range of analgesic doses of tramadol has no respiratory depressant effect. Similarly, the gastro-intestinal motility is not modified. The cardiovascular effects are generally slight. The potency of tramadol is considered to be one-tenth to one-sixth that of morphine.

The precise mechanism of the analgesic properties of Acetaminophen is unknown and may involve central and peripheral effects.

Acetaminophen and Tramadol Hydrochloride Tablets USP is positioned as a step II analgesic in the WHO pain ladder and should be utilised accordingly by the physician.

DOSAGE AND ADMINISTRATION:

Posology

Adults and adolescents (12 years and older)

The use of Acetaminophen and Tramadol Hydrochloride Tablets USP should be restricted to patients whose moderate to severe pain is considered to require a combination of Tramadol and Acetaminophen.

An initial dose of two tablets of Acetaminophen and Tramadol Hydrochloride Tablets USP is recommended. Additional doses can be taken as needed, not exceeding 8 tablets (equivalent to 300 mg tramadol and 2600 mg Acetaminophen) per day.

The dosing interval should not be less than six hours.

Children

Treatment is not recommended in children below the age of 12 years.

Elderly patients

The usual dosages may be used although it should be noted that in volunteers aged over 75 years the elimination half life of tramadol was increased by 17% following oral administration. In patients over 75 years old, it is recommended that the minimum interval between doses should be not less than 6 hours, due to the presence of tramadol.

Renal insufficiency and hepatic insufficiency

Because of the presence of tramadol, the use of Acetaminophen and Tramadol Hydrochloride Tablets USP is not recommended in patients with severe renal insufficiency and severe hepatic impairment.

Method of administration

Oral use

Tablets must be swallowed whole, with a sufficient quantity of liquid. They must not be broken or chewed.

CONTRAINDICATION:

- Hypersensitivity to tramadol, Acetaminophen or to any of the excipients of the medicinal product,
- acute intoxication with alcohol, hypnotic drugs, centrally-acting analgesics, opioids or psychotropic drugs

SPECIAL WARNING AND PRECAUTION FOR USE:

Warnings:

- In adults and adolescents 12 years and older. The maximum dose of 8 tablets of Acetaminophen and Tramadol Hydrochloride Tablets USP should not be exceeded
- In severe renal insufficiency (creatinine clearance <10 ml/mm), Acetaminophen and Tramadol Hydrochloride Tablets USP is not recommended.
- In patients with severe hepatic impairment Acetaminophen and Tramadol Hydrochloride Tablets USP should not be used.
- In severe respiratory insufficiency, Acetaminophen and Tramadol Hydrochloride Tablets USP is not recommended.

Precautions for use

Acetaminophen and Tramadol Hydrochloride Tablets USP should be used with caution in opioid dependent patients, or in patients with cranial trauma, in patients prone to convulsive disorder, biliary tract disorders, in a state of shock, in an altered state of consciousness for unknown reasons, with problems affecting the respiratory center or the respiratory function, or with an increased intracranial pressure.

Acetaminophen in overdosage may cause hepatic toxicity in some patients.

INTERACTION WITH OTHER MEDICINE AND CONCOMITANT USE:

Concomitant use is contraindicated with:

Non-selective MAO Inhibitors

Risk of serotoninergic syndrome: diarrhoea, tachycardia, sweating, trembling, confusion, even coma.

Selective-A MAO Inhibitors

Extrapolation from non-selective MAO inhibitors

Risk of serotoninergic syndrome: diarrhoea, tachycardia, sweating, trembling, confusion, even coma.

Concomitant use is not recommended with:

Alcohol

Alcohol increases the sedative effect of opioid analgesics.

Carbamazepine and other enzyme inducers

Risk of reduced efficacy and shorter duration due to decreased plasma concentrations of tramadol.

Opioid agonists-antagonists (buprenorphine, nalbuphine, pentazocine)

PREGNACY AND LACTATION:

Pregnancy

Since Acetaminophen and Tramadol Hydrochloride Tablets USP is a fixed combination of active ingredients including tramadol, it should not be used during pregnancy.

Data regarding Acetaminophen:

Epidemiological studies in human pregnancy have shown no ill effects due to Acetaminophen used in the recommended dosages.

Data regarding Tramadol:

Tramadol should not be used during pregnancy as there is inadequate evidence available to assess the safety of Tramadol in pregnant women. In neonates it may induce changes in the respiratory rate which are usually not clinically relevant.

Lactation:

Since Acetaminophen and Tramadol Hydrochloride Tablets USP is a fixed combination of active ingredients including tramadol, it should not be ingested during breast feeding.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

Tramadol may cause drowsiness or dizziness, which may be enhanced by alcohol or other CNS depressants. If affected, the patient should not drive or operate machinery.

UNDESIRABLE EFFECT:

Undesirable effects that may occur during treatment with Tramadol hydrochloride/Acetaminophen are classified into the following groups in order of frequency:

- very common (⩾1/10),
- common (⩾1/100 to <1/10),
- uncommon (⩾1/1,000 to <1/100),
- rare (⩾1/10,000 to <1/1,000),
- very rare (<1/10,000), not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The most commonly reported undesirable effects during the clinical trials performed with the Acetaminophen/tramadol combination were nausea, dizziness and somnolence, observed in more than 10% of the patients.

Cardiac disorders:

- Uncommon: hypertension, palpitations, tachycardia, arrythmia.

Nervous system disorders:

- Very common: dizziness, somnolence
- Common: headache trembling
- Uncommon: involuntary muscular contractions, paraesthesia, tinnitus

Psychiatric disorders:

- Common: confusion, mood changes (anxiety, nervousness, euphoria), sleep disorders
- Uncommon: depression, hallucinations, nightmares, amnesia

OVERDOSE:

Acetaminophen and Tramadol Hydrochloride Tablets USP is a fixed combination of active ingredients. In case of overdose, the symptoms may include the signs and symptoms of toxicity of tramadol or Acetaminophen or of both these active ingredients.

INCOMPATIBILITY:

Not Applicable.

SHELF LIFE:

3 years

PACKAGING:

10 tablets are packed in Alu-Alu Blister and such 10 blisters are packed in a printed carton along with pack insert.

STORAGE CONDITION:

Store in dry place below 30°C. Keep out of reach of children.

IMPORTED BY:

Galaxy Pharma Co. Ltd.
Cambodia.

MANUFACTURED BY:

Cian Health Care Pvt. Ltd.
Khasra No.: 248, Village Sisona, Bhagwanpur,
Roorkee, Haridwar, Uttarakhand, India.