1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

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PROPRIETARY NAME AND DOSAGE FORM

TRAMASPEN 50 mg (capsule)

COMPOSITION

Each capsule of TRAMASPEN 50 mg contains 50 mg of tramadol hydrochloride.

Excipients:

Colloidal silicon dioxide, dibasic calcium phosphate dihydrate, gelatine, magnesium stearate, titanium dioxide (C. I. 77891)

Sugar free

CATEGORY AND CLASS

A 2.9 Other analgesics

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Tramadol hydrochloride is a centrally-acting synthetic opioid analgesic binding to specific opioid receptors. It is a non-selective, pure agonist at mu (μ), delta (δ) and kappa (κ) opioid receptors with a higher affinity for the μ receptor. Other mechanisms, which may contribute to its analgesic effect, are inhibition of neuronal re-uptake of noradrenaline and enhancement of serotonin release.

Tramadol hydrochloride does not promote histamine release.

Pharmacokinetic properties

Tramadol hydrochloride is readily absorbed following oral administration. Oral bioavailability is approximately 68 % after a single dose and increases to 90 % at steady state. Onset of action is dose dependent but generally occurs within one hour of dosing, peaking within 2 to 3 hours. Duration of analgesia is about 6 hours. The rate or extent of absorption is not significantly affected by co-administration with food.

The bioavailability of tramadol hydrochloride after intramuscular injection or intravenous administration is the same; the mean peak serum concentration is achieved after 45 minutes. Tramadol hydrochloride is primarily metabolised in the liver (90 %) with one of its metabolites, mono-O-desmethyltramadol (M1), being 2 to 4 times as potent as the parent compound.

Tramadol hydrochloride has a linear pharmacokinetic profile within the therapeutic dosage range.

Tramadol hydrochloride and its metabolites are excreted mainly in the urine.

The elimination half-life is 5 to 7 hours, but is prolonged in impaired hepatic and renal function.

Tramadol hydrochloride crosses the blood-brain and placental barrier. Small amounts are excreted in breast milk unchanged or as the metabolite M1.

INDICATIONS

TRAMASPEN 50 mg is indicated for:

- the management of moderate to moderately severe pain.

CONTRAINDICATIONS

TRAMASPEN 50 mg is contraindicated in:

- Hypersensitivity to tramadol hydrochloride or opioids.
- Acute intoxication with alcohol, hypnotics, analgesic opioids or psychotropic medicines (due to the risk of respiratory depression).
- Patients taking monoamine oxidase (MAO) inhibitors or within two weeks of their discontinuation (see INTERACTIONS).
- Narcotic withdrawal treatment.
- Respiratory depression especially in the presence of cyanosis and excessive bronchial secretions.
- Increased intracranial pressure or central nervous depression due to head injury or cerebral disease.
- Pregnancy and lactation.

WARNINGS AND SPECIAL PRECAUTIONS

- Avoid the use of TRAMASPEN 50 mg in patients with a history of addiction, as physical dependence of the morphine-type may develop. Reinstatement of physical dependence in patients that have previously been dependent, may occur with TRAMASPEN 50 mg.
- Use with caution in patients with a history of epilepsy or those susceptible to seizures (e.g. patients taking neuroleptics and other medicines that reduce the seizure threshold).
- Use with caution in patients with renal or hepatic impairment and avoid if severe.
- The possibility of respiratory depression cannot be excluded if the recommended dose

is exceeded or other centrally depressant medicines are given concomitantly.

- TRAMASPEN 50 mg should not be used for the treatment of minor pain.

Effects on ability to drive and use machines

The administration of TRAMASPEN 50 mg concurrently with other central nervous system medicines is likely to intensify and prolong CNS effects (see INTERACTIONS). Patients should be warned not to operate machinery or drive a car while using TRAMASPEN 50 mg.

INTERACTIONS

Monoamine oxidase inhibitors (MAOIs)

Because of its inhibitory effect on serotonin uptake, TRAMASPEN 50 mg should not be used concomitantly with MAOIs or within 14 days after discontinuing such treatment (see CONTRAINDICATIONS).

Central nervous system (CNS) depression-producing medications, including alcohol and anaesthetics

Caution is recommended because concurrent use may potentiate the CNS depressant effects. The duration of anaesthesia may be prolonged when TRAMASPEN 50 mg is combined with barbiturates.

Carbamazepine

Serum concentrations of TRAMASPEN 50 mg are reduced by carbamazepine, resulting in diminished analgesic activity of TRAMASPEN 50 mg. Inhibitors of CYP3A4 such as ketoconazole and erythromycin may inhibit the metabolism of TRAMASPEN 50 mg.

HUMAN REPRODUCTION

The safety of TRAMASPEN 50 mg in pregnancy and lactation has not been established (see

CONTRAINDICATIONS).

DOSAGE AND DIRECTIONS FOR USE

The dosage should be adjusted to the intensity of pain and the individual's response to the analgesic action of TRAMASPEN 50 mg. TRAMASPEN 50 mg should not be used for the treatment of minor pain.

Adults and children over the age of 14 years

Initial dose of 50 mg, followed by 100 mg twice daily.

The dose may be increased to 150 mg or 200 mg twice daily.

Elderly

The usual doses may be used except in patients 75 years of age and over. A downward adjustment of the dose and/or prolongation of the interval between doses are recommended.

Renal impairment

The elimination of TRAMASPEN 50 mg may be prolonged. The usual initial dose should be used, but for patients with creatinine clearance < 30 ml/min, the dosage interval should be increased to 12 hours.

Hepatic impairment

The elimination of TRAMASPEN 50 mg may be prolonged. The usual initial dose should be used but in severe hepatic impairment, the dosage interval should be increased to 12 hours.

Duration of treatment

Under no circumstances should TRAMASPEN 50 mg be given for longer than absolutely necessary. If the nature and severity of the disease require long-term pain treatment with

TRAMASPEN 50 mg, evaluation should be carried out initially and at regular intervals to assess efficacy, adverse events, and the need for further treatment.

SIDE EFFECTS

Immune system disorders

Less frequent: anaphylaxis and anaphylactoid reactions. These reactions may occur after the first dose.

Frequency not known: angioedema, bronchospasm. These reactions may occur after the first dose. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome have been reported.

Nervous system disorders

Frequent: drowsiness, dizziness, headache.

Less frequent: confusion, hallucinations, seizures (see WARNINGS AND SPECIAL PRECAUTIONS), amnesia, paraesthesia, syncope.

Frequency not known: fatigue, sedation.

Eye disorders

Less frequent: blurred vision.

Cardiac disorders

Less frequent: flushing, syncope, tachycardia, postural hypotension.

Frequency not known: bradycardia, cardiovascular collapse.

Gastrointestinal disorders

Frequent: nausea, vomiting, dry mouth, dyspepsia, constipation, diarrhoea, anorexia, abdominal pain.

Hepato-biliary disorders

Frequency not known: increase in liver enzymes.

Skin and subcutaneous tissue disorders

Frequent: skin rashes, pruritus, sweating (especially when IV administration is too rapid).

Less frequent: vesicles, urticaria.

Renal and urinary disorders

Less frequent: urinary retention, urinary frequency.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Symptoms

Symptoms of overdosage are typical of opioids, and include pinpoint pupils, slow heartbeat, slow or troubled breathing, weakness, seizures, cold, clammy skin (see SIDE EFFECTS).

Treatment

Supportive measures such as maintaining the patency of the airway and maintaining cardiovascular function should be instituted. Treatment of restlessness is symptomatic and supportive.

Naloxone should be used to reverse some, but not all, symptoms caused by overdosage with TRAMASPEN 50 mg. Administration of naloxone should be done with caution because it may precipitate seizures.

Diazepam has been found to be effective in treating convulsions caused by TRAMASPEN 50 mg toxicity.

Haemodialysis is not recommended in overdose, since it removes less than 7 % of the administered dose of TRAMASPEN 50 mg in a 4-hour dialysis period.

IDENTIFICATION

White opaque hard gelatin capsule, containing a white odourless powder.

PRESENTATION

20, 30, 50 or 100 capsules are packed in a white, opaque polyvinylchloride film sealed with an aluminium foil backing. There are 10 capsules per blister strip and one or more blister strips are packed in an outer cardboard carton together with a leaflet.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light, heat and moisture.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

42/2.9/0967

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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