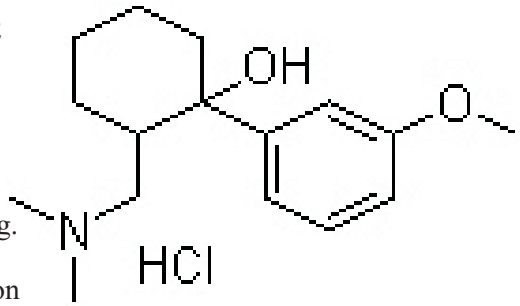
Taj Pharmaceuticals Ltd.

Tramadol Hcl

CAS No. : 22204-88-2

Chemical data

Molecular Formula C16H25NO2.HCl;C16H26ClNO2
Molecular Weight 299.84
CAS Registry Number 22204-88-2



Pharmacokinetic data

Bioavailability 68–72% Increases with repeated dosing.
Protein binding 20%
Metabolism Hepatic demethylation and glucuronidation
Half life 5–7 hours
Excretion Renal

DOSAGE

For patients with moderate to moderately severe chronic pain not requiring rapid onset of analgesic effect, the tolerability of Tramadol Hcl can be improved by initiating therapy with the following titration regimen: Tramadol Hcl should be started at 25 mg/day qAM and titrated in 25 mg increments as separate doses every 3 days to reach 100 mg/day (25 mg q.i.d.). Thereafter the total daily dose may be increased by 50 mg as tolerated every3days to reach 200 mg/day (50 mg q.i.d.). After titration, Tramadol Hcl 50 to 100 mg can be administered as needed for pain relief every 4 to 6 hours not to exceed 400 mg/day.

For the subset of patients for whom rapid onset of analgesic effect is required and for whom the benefits outweigh the risk of discontinuation due to adverse events associated with higher initial doses, Tramadol Hcl 50 mg to 100 mg can be administered as needed for pain relief every four to six hours, not to exceed 400 mg per day.
Individualization of Dose
Good pain management practice dictates that the dose be individualized according to patient need using the lowest beneficial dose. Studies with tramadol in adults have shown that starting at the lowest possible dose and titrating upward will result in fewer discontinuations and increased tolerability.

In all patients with creatinine clearance less than 30 mL/min, it is recommended that the dosing interval of Tramadol Hcl be increased to 12 hours, with a maximum daily dose of 200 mg. Since only 7% of an administered dose is removed by hemodialysis, dialysis patients can receive their regular dose on the day of dialysis.
The recommended dose for adult patients with cirrhosis is 50 mg every 12 hours.
In general, dose selection for an elderly patient over 65 years old should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequencyof decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy. For elderly patients over 75 years old, total dose should not exceed 300 mg/day.

SIDE EFFECTS

Side effects reported with Tramadol Hcl include constipation, somnolence (sleepiness) and increased sweating. Tramadol Hcl should not be used concomitantly with alcohol. Since tramadol can reinitiate physical dependence, Tramadol Hcl is not recommended for subjects disposed to drug or alcohol abuse.

Seizures have been reported in subjects receiving tramadol treatment. Data indicates that the risk of seizures is increased with doses of tramadol above the recommended range. Tramadol use has been shown to increase seizure risk in subjects taking the following medications

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* Selective serotonin reuptake inhibitors
* Tricyclic antidepressants
* Opioids

Additionally, tramadol may enhance the risk of seizures in subjects taking the following:

* MAO inhibitors
* Neuroleptics
* Other drugs that reduce the seizure threshold

PRECAUTIONS

Acute Abdominal Conditions

The administration of Tramadol Hcl may complicate the clinical assessment of patients with acute abdominal conditions. Use in Renal and Hepatic Disease

Impaired renal function results in a decreased rate and extent of excretion of tramadol and its active metabolite, M1. In patients with creatinine clearances of less than 30 mL/min, dosing reduction is recommended Metabolism of tramadol and M1 is reduced in patients with advanced cirrhosis of the liver. In cirrhotic patients, dosing reduction is recommended

With the prolonged half-life in these conditions, achievement of steady-state is delayed, so that it may take several days for elevated plasma concentrations to develop.

Carcinogenesis, Mutagenesis, Impairment of Fertility as light, but statistically significant, increase in two common murine tumors, pulmonary and hepatic, was observed in a mouse carcinogenicity study, particularly in aged mice. Mice were dosed orally up to 30 mg/kg (90 mg/m2 or 0.36 times the maximum daily human dosage of 246 mg/m2)for approximately two years, although the study was not done with the Maximum Tolerated Dose. This finding is not believed to suggest risk in humans. No such finding occurred in a rat carcinogenicity study (dosing orally up to 30 mg/kg,180 mg/m2, or 0.73 times the maximum daily human dosage).

Tramadol was not mutagenic in the following assays:Ames Salmonella microsomal activation test, CHO/HPRT mammalian cell assay, mouse lymphoma assay (in the absence of metabolic activation), dominant lethal mutation tests in mice, chromosome aberration test in Chinese hamsters, and bone marrow micronucleus tests in mice and Chinese hamsters. Weakly mutagenic results occurred in the presence of metabolic activation in the mouse lymphoma assay and micronucleus test in rats. Overall, the weight of evidence from these tests indicates that tramadol does not pose a genotoxic risk to humans.

Labor and Delivery

Tramadol Hcl should not be used in pregnant women prior to or during labor unless the potential benefits outweigh the risks. Safe use in pregnancy has not been established. Chronic use during pregnancy may lead to physical dependence and post-partum withdrawal symptoms in the newborn (see Drug Abuse And Dependence).Tramadol has been shown to cross the placenta. The mean ratio of serum tramadol in the umbilical veins compared to maternal veins was 0.83 for 40 women given tramadol during labor.

The effect of Tramadol Hcl , if any, on the later growth, development, and functional maturation of the child is unknown.

Nursing Mothers

Tramadol Hcl is not recommended for obstetrical preoperative medication or for post-delivery analgesia in nursing mothers because its safety in infants and newborns has not been studied. Following a single IV 100 mg dose of tramadol, the cumulative excretion in breast milk within 16 hours postdose was 100 ug of tramadol (0.1% of the maternal dose) and 27 ug of M1.

Pediatric Use

The safety and efficacy of Tramadol Hcl in patients under 16 years of age have not been established. The use of Tramadol Hcl in the pediatric population is not recommended.

DRUG DESCRIPTION

Tramadol is used to treat moderate and severe pain and most types of neuralgia, including trigeminal neuralgiaIt has been suggested that tramadol could be effective for alleviating symptoms of depression and anxiety because of its action on the noradrenergic and serotonergic systems, the involvement of which appear to play a part in its ability to alleviate the perception of pain. However, health professionals have not yet endorsed its use on a large scale for disorders such as this.

The molecular weight of tramadol hydrochloride is 299.8. Tramadol hydrochloride is a white, bitter, crystalline and odorless powder. It is readily soluble in water and ethanol and has a pKa of 9.41. The n-octanol/water log partition coefficient (logP) is 1.35 at pH 7. Tramadol Hcl tablets contain 50 mg of tramadol hydrochloride and are white in color. Inactive ingredients in the tablet are corn starch, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, sodium starch glycolate, titanium dioxide and wax.

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In addition, it also contains the following inactive ingredients:
hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, pregelatinized starch, sodium starch glycolate and titanium dioxide.

Note /Government Notification: These chemicals are designated as those that are used in the manufacture of the controlled substances and are important to themanufacture of the substances. For any (Control Substance) products Import and Export *** subjected to your country government laws /control substance ACT.

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The Controlled Substances Act (CSA) was enacted into law by the Congress of the United States as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970.[1] The CSA is the federal U.S. drug policy under which the manufacture, importation, possession, use and distribution of certain substances is regulated. The Act also served as the national implementing legislation for the Single Convention on Narcotic Drugs

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