PATRIOT
Pharmaceuticals Corp.

TRAMADOL HCl

TDL®

Analgesic

FORMULATION:
Each capsule contains: Tramadol hydrochloride 50mg
Each mL of Solution for Injection contains: Tramadol hydrochloride 50mg

INDICATIONS:
Moderate to severe acute and chronic pain, painful diagnostic procedures and surgery.

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

Tramadol has an antitussive effect. In contrast to morphine, analgesic doses of tramadol over a wide range have no respiration-depressant effect. Also, gastrointestinal motility is less affected. Effects on the cardiovascular system tends to be slight. The potency of tramadol is reported to be 1/10 (one-tenth) to 1/6 (one-sixth) that of morphine.

PHARMACOKINETICS: Tramadol is readily absorbed following oral administration but is subject to first-pass metabolism. Tramadol is metabolized by N - and O - demethylation and glucuronidation or sulfation in the liver. The metabolite O - desmethyltramadol is pharmacologically active. Tramadol is excreted mainly in the urine predominantly as metabolites. Tramadol is widely distributed, crosses the placenta, and appears in small amounts in breast milk. The elimination half-life following oral administration is about 6 hours.

METABOLISM: Production of the active metabolite O - desmethyltramadol is dependent on the cytochrome P450 isoenzyme CYP2D6, which exhibits genetic polymorphism. Concomitant administration with specific inhibitors of this enzyme, such as quinidine, may increase concentrations of tramadol and lower concentrations of its active metabolite but the clinical consequence of this effect are unclear.

INCOMPATIBILITIES: An injection of tramadol hydrochloride 50mg per mL is reported to be incompatible with injections of diazepam, diclofenac sodium, indometacin, midazolam and piroxicam if mixed in the same syringe.

DEPENDENCE AND WITHDRAWAL: Tramadol may have lower potential for producing dependence than morphine.

CONTRAINDICATIONS
Tramadol HCl is contraindicated in patients with hypersensitivity to the active substance or any of the excipients and in patients with acute intoxication with alcohol, hypnotics, analgesics, opioids or other psychotropic medicinal product.

ADVERSE EFFECTS: Common side effects of opoid analgesics like tramadol are nausea, vomiting, constipation, drowsiness and confusion; tolerance of these (except confusion) generally develops with long-term use.

Tramadol may produce fewer typical opoid adverse effects such as respiratory depression and constipation. In addition to hypotension, hypertension has occasionally occurred. Anaphylaxis, hallucinations and confusion have also been reported

EFFECTS ON THE RESPIRATORY SYSTEM: Respiratory depression has been reported after tramadol infusion anesthesia although in a postoperative study tramadol had no significant respiratory depressant effect when equianalgesic doses of morphine, pentazocine, pethidine, piritramide and tramadol were compared.

PRECAUTIONS: Tramadol should be used with caution in patients with renal or liver impairment and should be avoided if renal impairment is severe. Removal by haemodialysis is reported to be very slow.

Tramadol should be used with care in patients with a history of epilepsy or those susceptible to seizures.

ANESTHESIA: Do not take tramadol during light planes of general anesthesia because of possible intra-operative awareness, although it may be used intra-operatively provided anesthesia is maintained by the continuous administration of a potent volatile or intraveneous anesthetic.

INTERACTIONS: Carbamazepine is reported to diminish the analgesic activity of tramadol by reducing serum concentration. The risk of seizures is increased if tramadol is administered concomitantly with other drugs that have the potential to lower the seizure threshold.

Tramadol inhibits reuptake off nonadrenaline and serotonin and enhances serotonin release and there is the possibility that it may interact with other drugs that enhance monoaminergic neurotransmission including lithium, tricyclic antidepressants and selective serotonin reuptake inhibitors; it should not be given to patients receiving MAOIs or within 114 days of their discontinuation

Fertility, Pregnancy and Lactation

Pregnancy
Animal studies revealed that tramadol used at very high doses has effects on organ development, ossification and neonatal mortality. Tramadol crosses the placenta. There is inadequate evidence on the safety of tramadol in human pregnancy.

Therefore, tramadol should not be used in pregnant women.

Tramadol administered before or during birth does not affect uterine contractility. In neonates it may induce changes in the respiratory rate which are usually not clinically relevant. Chronic use during pregnancy may lead to neonatal withdrawal symptoms.

Breast-feeding
During lactation about 0.1% of the maternal dose is secreted into the milk. Tramadol is not recommended during breast-feeding.

Fertility
Animal studies did not show an effect of tramadol on fertility.

Effects on Ability to Drive and Use Machines

Even when taken according to instructions, tramadol may cause effects such as somnolence and dizziness and therefore may impair the reactions of drivers and machine operators.

CAUTION: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

USES AND ADMINISTRATION:

TDL *capsule*
The dosage depends on the intensity of the pain and the sensitivity of the individual patient. The total daily dosage by mouth should not exceed 400mg.
Usual doses by mouth are 50 to 100mg every 4 to 6 hours.

TDL *ampoule*
A dose of 50 to 100mg may be given every 4 to 6 hours by intravenous injection over 2 to 3minutes, or by intravenous infusion.
For treatment of postoperative 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 100 mg every 4 to 6 hours to total daily dose of 600mg

The dosage interval should be increased to 12 hours in patients with a creatinine clearance less than 30mL per minute. The maximum dose by mouth should not exceed 200mg daily in these patients.

Tramadol should not be given to patients with more severe renal impairment (creatinine clearance less than 10ml per minute). A dosage interval of 12 hours is also recommended in severe hepatic impairment.

OVERDOSAGE
The general emergency measures apply. Keep open the respiratory tract, maintain respiration and circulation depending on the symptoms. In case of intoxication with oral formulations, gastrointestinal decontamination with activated charcoal or by gastric lavage is only recommended within 2 hours after tramadol intake. Tramadol is minimally eliminated from the serum by hemodialysis or hemofiltration. Therefore, treatment of acute intoxication with Tramadol HCl with hemodialysis or hemofiltration alone is not suitable for detoxification

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph"

AVAILABILITY:
TDL capsule: Box of 50 capsules
TDL Ampoules: Box of 10 x 2mL ampoules

Registration Number: DR-XY16016; Amp (DR-XY17749)
Date of First Authorization: June 1993; Amp (April 2004)
Revision Date: August 2018

STORE AT TEMPERATURES NOT EXCEEDING 30°C

Manufactured for
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