JOLIVEL

(Opipramol Dihydrochloride Tablets)

COMPOSITION

Jolivel 50
Opipramol Dihydrochloride Tablets 50 mg

Each film coated tablet contains:
Opipramol Dihydrochloride……50mg
Excipients …… q.s
Approved colours used

Jolivel 100
Opipramol Dihydrochloride Tablets 100 mg

Each film coated tablet contains:
Opipramol Dihydrochloride……100mg
Excipients …… q.s
Approved colours used

DOSAGE FORM

Film coated tablet.

INDICATION

For the treatment of generalised anxiety disorder (GAD) and somatic disturbances.

DOSE AND METHOD OF ADMINISTRATION

Treatment must be observed by the physician.
The dosage in adults should be usually 1-2 tablets per day (in the morning and in the evening) according. The dosage may depend on the efficacy and tolerability up to once daily 50 mg - 100 mg and it can be reduced or increased up to 3 times daily. Children older than 6 years should receive 3 mg Opipramol/kg body weight. Since the experience with Opipramol tablets is limited in the pediatric dosage, this recommendation is only a framework directive.
Opipramol tablets should be taken with some liquid (water, fruit juice).
Since the effect of tablets Opipramol not abruptly occurs in appearance and gradually occurs, the drug should be taken regularly for at least 2 weeks.
Average treatment duration of 1-2 months is advisable.

USE IN SPECIAL POPULATIONS

Pregnancy and lactation
There is no data available on use of opipramol in pregnancy.

Animal studies do not indicate harmful effects of opipramol on embryonic development or fertility. Opipramol tablets should be prescribed during pregnancy especially in the first trimester unless clearly necessary.

Opipramol tablets should not be taken during lactation because the drug is excreted in small amounts into breast milk.

CONTRAINDICATIONS

Opipramol tablets are contraindicated in:

- Hypersensitivity to Opipramol Dihydrochloride, propyl 4-hydroxybenzoate, methyl 4-hydroxy benzoate or any of the other ingredients.
- Acute alcohol, sedatives, analgesics and psychotropic intoxication
- Acute urinary retention
- Acute delirium
- Untreated narrow angle glaucoma
- Prostatic hypertrophy with urinary retention
- Paralytic ileus
- Pre-existing higher-grade AV block or diffuse supraventricular or ventricular conduction disturbances
- Combination with MAO inhibitors.

WARNINGS AND PRECAUTIONS

Opipramol tablets should not be used in patients with prostate, liver, kidney diseases, brain damage of different etiologies, cerebrovascular insufficiencies, cardiac pre damage especially conduction damages, epilepsy and alcoholism. Patients with pre-existing heart block or other conduction disturbances should be under close ECG monitoring during treatment with Opipramol. Blood disorders such as neutropenia, agranulocytosis may occur. Thus, blood counts should be monitored during treatment with Opipramol tablets. Opipramol tablets may cause fever, flu like symptoms, angina, and hypersensitivity reactions including delayed reactions. Opipramol tablets should be discontinued if any such reactions and symptoms occur. In case of long-term treatment with opipramol, it is advisable to check the liver function tests. Patients with rare hereditary problems such as galactose intolerance, Lapp lactase deficiency, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take Opipramol tablets.

DRUG INTERACTIONS

The therapy with Opipramol indicates an additional therapy with neuroleptics, hypnotics and tranquilizers (e.g. barbiturates, benzodiazepines). Therefore, it should be noted that some specific reactions, particularly CNS depressant effects could be enhanced and an intensification of common side effects may occur. If necessary the dosage may be reduced. Its effect can also be enhanced by strong anticholinergic, such as Antiparkinsonian agents and Phenothiazines.

Concomitant treatment with serotonin reuptake inhibitors with opipramol may lead to additive effects on the serotonergic system. Fluoxetine and fluvoxamine may thus lead to an increase in the plasma concentrations of tricyclic psychotropic drugs and side effects. Hence if necessary its dosage should be reduced.
The combination of opipramol with alcohol can cause drowsiness.
MAO Inhibitors should be discontinued at least 14 days prior to treatment with opipramol tablets. The same applies to Opipramol tablets when MAO Inhibitors are administered.

The concomitant use of beta-blockers (eg, propranolol), antiarrhythmics class Ic and drugs from the group of tricyclic antidepressants and drugs that affect the microsomal enzyme system of the liver, can lead to change in the plasma concentrations of these medicinal products and of opipramol. Barbiturates and anticonvulsants may reduce the plasma concentration of opipramol tablets and thus attenuate the therapeutic effect. Co-administration of antipsychotic drugs (e.g., haloperidol, risperidone) may increase the plasma concentration of opipramol tablets. If necessary, appropriate dose adjustments should be made.

Effect on ability to drive and use machines
This medicine may change responsiveness of even normal functions. The ability to participate actively, drive or operate machinery is also impaired. This applies even more in combination with alcohol.

UNDESIRABLE EFFECTS
Frequency:-
Common = 1% to <10%; uncommon = 0.1% to <1%, rare = 0.01% to <0.1%
Very rare: <0.01%

	Common	Uncommon	Rare	Very rare
Nervous system, autonomic nervous system, psyche	Especially at the beginning of treatment fatigue, dry mouth, stuffy nose	Dizziness, drowsiness, micturition disorders, accommodation disturbances, tremor, weight gain, thirst.	Agitation, headache, paresthesia, especially in the elderly confusion and delirium, especially when abrupt withdrawal, restlessness, sweating and insomnia	Seizures, motor disorders (akathisia, dyskinesia), ataxia, polyneuropathy, glaucoma seizures, and anxiety.
Skin and appendages		Allergic skin reactions (rash, urticaria)	edema	baldness

Hormone system		Ejaculation disorders, erectile impotence	galactorrhea, (excessive flow of milk)	
Urogenital system			Urinary retention	
Gastrointestinal system		constipation	Stomach discomfort, dysgeusia, paralytic ileus, particularly when abrupt withdrawal of a long-term, high-dose therapy Nausea and vomiting	
Hepatobiliary System		Transient increases in liver enzyme activities		Severe hepatic impairment, after long-term treatment jaundice and chronic liver damage
Cardiovascular system	Especially early in treatment hypotension and orthostatic dysregulation	Tachycardia, palpitations	Collapse states, conduction disturbances, reinforcing an existing heart failure	
Blood system			Blood disorders, especially leucopenia	Agranulocytosis

OVERDOSE

Symptoms of intoxication

Drowsiness, dizziness insomnia, restlessness, coma, stupor, temporary confusion, increased anxiety, ataxia, convulsions, oliguria, anuria, tachycardia / bradycardia, arrhythmia, atrioventricular block, hypotension, shock, respiratory depression and rarely cardiac arrest.

Therapy of intoxication

A specific antidote is not available. The pollutant should be removed by vomiting and / or gastric lavage. An introduction to clinical treatment securing the vital functions should be

carried out. Cardiovascular monitoring should be monitored continuously for at least 48 hours.

In case of overdose the following measures should be taken:

- Respiratory insufficiency: intubation and artificial respiration
- Severe hypotension: Appropriate storage, plasma expander, dopamine or dobutamine in a drip.
- Cardiac arrhythmias: Individual treatment; possibly pacemaker; Compensating low potassium levels and possible acidosis.
- Convulsions: diazepam administration of i.v. or another anticonvulsant agent such as Phenobarbital or paraldehyde (Beware any reinforcement of existing respiratory insufficiency, hypotension or coma by these substances).

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group
Sedatives /anxiolytics

Opipramol has high affinity for the sigma binding sites (type 1 and type 2) and histamine antagonist receptors of type 1. The affinities for the serotonin receptors of type 2A, dopamine type 2 receptors and the alpha-adrenergic receptors are low to moderate. In contrast to the structurally related tricyclic antidepressants, opipramol has little anti cholinergic activity and does not inhibit the reuptake of serotonin or nor epinephrine.

About the sigma receptors in modulating NMDA, protective effects against ischemia-induced neuronal loss in the hippocampus region were demonstrated in animal experiments. Similarly modulating effects in the serotonergic and noradrenergic system are described for sigma ligands. Opipramol is like other, more selective sigma ligands active in behavioral pharmacological models that are indicative of anxiolysis, and has relatively lower activity in the swimming test in rats, which is used as a screening method for potential antidepressants.

In humans Opipramol acts as sedative, anxiolytic and mood-lifting agent.

Pharmacokinetic properties

Following oral administration, opipramol is rapidly and completely absorbed. A partial metabolism to Deshydroxyethyl-Opipramol occurs in the liver. Plasma protein binding is approximately 91%; the volume of distribution is about 10 l / kg. The elimination half-life is about 11 hours.

Opipramol is metabolized primarily by the CYP2D6 isoenzyme. In patients with CYP2D6 deficiency (poor metabolizer), the maximum plasma concentration of opipramol will be up to

2.5 times higher than normal metabolizers. Upon chronic administration, the eliminations are not reduced so that an accumulation of opipramol even in the poor metabolizers is not expected.

Preclinical safety data

The acute toxicity in experimental animals is relatively low. Symptoms of poisoning affect mainly the central nervous system; sub chronic and chronic administration of very high doses cause CNS symptoms, liver and lung damage, skin and coat changes, as well as species-specific cataract formation.

In vitro and in vivo studies showed no evidence of mutagenic potential. Animal studies brought no evidence of impairment of fertility by opipramol. In embryotoxicity studies, teratogenic effects were not observed, but at maternal toxic dose range embryotoxic effects were observed. Studies on peri- and postnatal toxicity were not performed.

EXPIRY DATE
Do not use later than the date of expiry.

PACKAGING INFORMATION
Blister (ALU-PVC) of 10 Tablets.

STORAGE AND HANDLING INSTRUCTIONS
Store below 30°C, Protected from light and moisture.

MARKETED BY

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IN/ JOLIVEL 50,100mg/Aug-15/01/PI