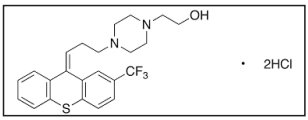
Pentoxol
Tablets*

پینٹوکسل ٹیبلٹس

COMPOSITION:
Each film coated tablet contains Flupentixol As Dihydrochloride ……..... 0.5,1 and 3 mg

DESCRIPTION
PENTOXOL is an antipsychotic drug available as 0.5,1 and 3mg. Its Chemical name is 2-trifluoromethyl-9-[2-hydroxyethyl)- piperazin-1-yl]propylidene]thioxanthene dihydrochloride. Molecular Formula is C23H25F3N2OS2HCl



CLINICAL PHARMACOLOGY
Flupentixol is a thioxanthene derivative with antipsychotic properties. The exact mechanism of action of flupentixol has not been established. Its effects resemble those of the phenothiazine, fluphenazine, in that it belongs among the antipsychotic drugs which are less likely to cause sedation and hypotension, but have greater propensity for producing extrapyramidal reactions.
Pharmacokinetics:
The kinetics is linear.
Absorption: Flupentixol dihydrochloride is well absorbed from the gastrointestinal tract. Oral bioavailability is about 40%. Based upon radioisotope monitoring in man, the drug reaches maximum serum concentrations within 3 to 8 hours. Steady state plasma levels are achieved in about 7 days. The mean minimum steady state level corresponding to 5 mg flupentixol orally once-a-day was about 1.7 ng/ml (3.9 nmol/l).
Distribution: The highest levels of flupentixol as reflected by radioactivity count are found in the lungs, liver, and spleen, while concentrations in the brain are considerably lower, and only a little higher than concentrations found in the blood. The apparent volume of distribution (Vd)β is about 14.1 l/kg. The plasma protein binding is about 99 %.
Metabolism: Flupentixol is metabolized by sulfoxidation, dealkylation (splitting of the distal ethanolic group in the side chain) and conjugation to glucuronic acid. The metabolites of flupentixol are devoid of psychopharmacological activity. In the rat, flupentixol dihydrochloride is metabolized in the liver to the sulphoxide and glucuronide derivatives. In the feces, it is found mainly in the unchanged state and in the urine as the unchanged drug with the sulphoxide and glucuronide derivatives.
Excretion: The more hydrophilic metabolites, sulfoxides and glucuronides are excreted with urine, the more lipophilic ones, flupentixol and dealkyl-flupentixol, with feces. Quantitatively, the fecal excretion dominates. The elimination half-life (T½ β) is about 35 hours and the mean systemic clearance (Cls) is about 0.29 l/min.

INDICATIONS AND USAGE
PENTOXOL tablets (flupentixol dihydrochloride) is indicated for maintenance therapy of chronic schizophrenic patients whose main manifestations do not include
- excitement
- agitation
- hyperactivity

Geriatrics (> 65 years of age): The pharmacokinetics, safety, and efficacy of flupentixol in elderly patients with schizophrenia have not been systematically evaluated in clinical trials. Caution should thus be exercised in dose selection for an elderly patient, recognizing the more frequent hepatic, renal and cardiac dysfunctions in this population.
Pediatrics (< 18 years): Since the safety and efficacy of flupentixol in children has not been established, its use is not recommended in the pediatric age group.

CONTRAINDICATIONS
Patients with known hypersensitivity to thioxanthenes, flupentixol or to any ingredient in the formulation or component of the container. The possibility of crosssensitivity between the thioxanthenes and phenothiazine derivatives should be considered.
Alcohol, barbiturate or opiate intoxication.
Patients with CNS depression due to any cause, comatose states, suspected or established subcortical brain damage or circulatory collapse.
Patients with liver damage, cerebrovascular or renal insufficiency, and severe cardiovascular disorders. Flupentixol is not indicated for the management of severely agitated psychotic patients, psychoneurotic patients or geriatric patients with confusion and/or agitation. As with

CLINICAL PHARMACOLOGY

Organ/Organ System	Adverse Reaction
Autonomic Nervous System	Dry mouth, blurred vision, constipation, excessive salivation, excessive perspiration, nausea, difficulty in micturition, dizziness, palpitations and fainting
Central Nervous System	Extrapyramidal symptoms, including hypo- and hyperkinetic states, tremors, pseudoparkinsonism, dystonia, hypertonia, akathisia, oculogyric crises, opisthotonos, hyperreflexia and tardive dyskinesia
Metabolic and Endocrine	Weight change, galactorrhea, elevation in serum prolactin levels, impotence, loss of libido, and sexual excitement have been reported with flupentixol.
Miscellaneous	Patients should be advised of the risk of severe constipation during flupentixol treatment, and that they should tell their doctor if constipation occurs or worsens, as they may need laxatives

DRUG INTERACTIONS
Flupentixol enhances the sedative response to alcohol and the effects of barbiturates and other CNS depressants. It should not be administered with high doses of hypnotics due to the possibility of potentiation.
Flupentixol should not be given concomitantly with guanethidine or similar acting compounds, since antipsychotic drugs such as flupentixol may block the antihypertensive effect of these compounds. Many antipsychotic and tricyclic antidepressant drugs may mutually inhibit the metabolism of each other.
Concomitant use of metoclopramide increases the risk of extrapyramidal symptoms.
Flupentixol may antagonize the effects of levodopa and dopamine agonists.

USE IN SPECIFIC POPULATION
Geriatrics (> 65 years of age): The pharmacokinetics, safety, and efficacy of flupentixol in elderly patients with schizophrenia have not been systematically evaluated in clinical trials. Caution should thus be exercised in dose selection for an elderly patient, recognizing the more frequent hepatic, renal and cardiac dysfunctions in this population.
Pregnant and Nursing Women: The safety of flupentixol in pregnancy and breastfeeding women has not been established. As flupentixol is found in breast milk in low concentrations, it is not likely to affect the infant when therapeutic doses are used.
Pediatrics (< 18 years): Since the safety and efficacy of flupentixol in children has not been established, its use is not recommended in the pediatric age group.
Reduced renal function: Based on the characteristics for elimination it is reasonable to assume that reduced kidney function is likely not to have much influence on the serum levels of parent drug.
Reduced hepatic function:
No data available.

WARNINGS AND PRECAUTIONS
Neuroleptic malignant syndrome (NMS) is a rare, sometimes fatal, neurological disorder that has been reported in association with antipsychotic drugs including flupentixol.

DOSAGE AND ADMINISTRATION
The dosage of PENTOXOL tablets should be individualized and adjusted according to the severity of symptoms and tolerance to the drug. The maintenance dose can usually be given as a single morning dose. The antipsychotic effect increases with increasing dosage; in addition some sedation should be anticipated.
PENTOXOL tablets The initial recommended dose of PENTOXOL tablets is one mg three times a day. This may be increased, if necessary, by one mg every 2 to 3 days until there is effective control of psychotic symptoms. The usual maintenance dosage is 3 to 6 mg daily in divided doses, although doses of up to 12 mg daily or more have been used in some patients. During the initial PENTOXOL tablet therapeutic period, disturbance of sleep may occur, especially in those patients who have previously received neuroleptics possessing a marked sedative effect. In this event, the evening dose of PENTOXOL tablets may be reduced.
Use in the Elderly: The use of flupentixol in elderly patients with schizophrenia has not been systematically evaluated. Caution should thus be exercised in dose selection for an elderly patient, recognizing the more frequent hepatic, renal and cardiac dysfunctions in this population. Hepatic Impairment: the use of flupentixol is contraindicated in patients with impaired liver function. Renal Impairment: the use of flupentixol is contraindicated in patients with impaired renal function.

OVERDOSAGE
Overdosage can be characterized by sedation, frequently preceded by extreme agitation, excitement, confusion, somnolence, coma, convulsions and hyperthermia/hypothermia. Extrapyramidal symptoms may develop, and respiratory and circulatory collapse may occur. ECG changes, QT prolongation, Torsades de Pointes, cardiac arrest and ventricular arrhythmias have been reported when flupentixol is administered in overdose together with drugs known to affect the heart. Treatment is symptomatic. An airway should be maintained. Severe hypotension calls for the immediate use of an I.V. vasopressor drug, such as levarterenol. Epinephrine should not be used, as a further lowering of blood pressure may result. Antiparkinsonian medication should be administered only if extrapyramidal symptoms develop. PENTOXOL (flupentixol dihydrochloride) tablets. In the case of PENTOXOL (flupentixol dihydrochloride) tablet overdose, gastric lavage should be carried out immediately and measures aimed at supporting the respiratory and cardiovascular systems instituted

STORAGE/PRECAUTIONS:
Store in a cool, dry and dark place between 15- 30 °C. Keep all medicines out of the reach of children. To be used on the prescription of Registered Medical Practitioners.

PRESENTATION:
PENTOXOL Tablets 0.5,1and 3 mg are available in packing containing 50 film coated tablets.
*Scotmann Specs.

خوراک: ڈاکٹر کی ہدایت کے مطابق۔

احتیاط: روشنی، نمی اور گرمی سے بچائیں۔ 15 سے 30 ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔ مستند ڈاکٹر کے نسخہ پر فروخت اور استعمال کریں۔

Complete Medical Information available only for doctors on request.

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Manufactured by: **SCOTMANN PHARMACEUTICALS**
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