Flupenscot Injection

فلوپین سکاٹ انجکشن

COMPOSITION: *Each ml contains:* Flupentixol Decanoate BP. .....40 mg.

DESCRIPTION: Flupentixol (Flupenscot) is a thioxanthene derivative with pronounced antipsychotic effect on intramuscular administration. Its chemical designation is cis(Z)-2-trifluoromethyl-9-(3-(4-(2-hydroxyethyl)-1-piperazinyl)-propylidene)-thioxanthene decanoic acid ester. The empirical formula is $C_{33}H_{43}F_3N_2O_2S$ and has a molecular weight of 588.82.

PHARMACOLOGY: *Pharmacodynamics:* Flupentixol is a thioxanthene derivative with antipsychotic properties.The antipsychotic effect of neuroleptics is normally related to their dopamine receptor blocking effect however the exact mechanism of action of Flupentixol has not been established. Flupentixol injection permits continuous antipsychotic treatment especially of those patients who are unreliable in taking the medication prescribed for them. Flupentixol injection thus prevents the frequent relapses caused by failure to take oral medication. *Pharmacokinetics:* The kinetics is linear. *Absorption:* The esterification of Flupentixol results in the slow release of the drug from the injection site with consequent prolongation of duration of action. In pharmacokinetic studies, while measuring Flupentixol blood levels peak concentrations of the drug were found between days 4 and 7, following intramuscular injections of 40 mg of Flupentixol 2% or 10%. It could still be detected in the blood three weeks after injection. *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 $(V_d)_\beta$ 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. Flupentixol injection is efficiently hydrolized in vivo to Flupentixol which is present in all tissues of the body. *Excretion:* With an estimated half-life of 3 weeks steady state conditions will be attained after about 3 months' repeated administration.

INDICATIONS: Flupenscot Injection is indicated for the treatment and maintenance therapy of schizophrenia and other related psychoses. Flupentixol is not recommended in state of excitement or overactivity, including mania.

CONTRAINDICATIONS: Flupentixol is contraindicated in case of:

- Patients with known hypersensitivity to thioxanthenes, Flupentixol or to any ingredient in the formulation or component of the container.
- Possibility of cross sensitivity 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. Flupentixol should not be used concomitantly with large doses of hypnotics due to the possibility of potentiation.

POSSIBLE ADVERSE EFFECTS: The following side effects are most pronounced in the beginning of the treatment and most of them usually wear off during continued treatment:

Very Common (in 1 or more out of 10 persons):

- Somnolence, akathisia, hyperkinesia, hypokinesia.
- Dry mouth.

Common (in more than 1 out of 100 persons and less than 1 out of 10 persons):

- Tachycardia, palpitations.
- Tremor, dystonia, dizziness, headache.
- Accommodation disorder, vision abnormalities.
- Dyspnoea.
- Salivary hypersecretion, constipation, vomiting, dyspepsia, diarrhoea.
- Urination disorder micturition disorder, urinary retention.
- Hyperhidrosis, pruritus.
- Myalgia.
- Increased appetite, increased weight.
- Asthenia.
- Insomnia, depression, nervousness, agitation, decreased libido.

As with other medicines that work in a way similar to Flupentixol, rare cases of the following side effects have been reported:

- QT prolongation (slow heart beat and change in the ECG).
- Ventricular arrhythmias, ventricular fibrillation, ventricular tachycardia.
- Torsades de Pointes.

In rare cases arrhythmias may have resulted in sudden death. Blood clots in the veins especially in the legs (symptoms include swelling, pain and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing. In elderly people with dementia, a small increase in the number of deaths has been reported for patients taking antipsychotics compared with those not receiving antipsychotics.

DRUG INTERACTIONS:

- Tricyclic antidepressant medicines.
- Guanethidine and similar medicines.
- Barbiturates.
- Medicines used to treat epilepsy.
- Levodopa and similar medicines.
- Metoclopramide.
- Piperazine.
- Medicines that cause a disturbed water or salt balance.
- Medicines known to increase the concentration of Flupentixol in the blood.

The following medicines should not be taken at the same time as Flupentixol:

- Medicines that change the heartbeat (quinidine, amiodarone, sotalol, dofetilide, erythromycin, terfenadine, astemizole, gatifloxacin, moxifloxacin, cisapride, lithium).
- Other antipsychotic medicines.
- Flupentixol may increase the sedative effects of alcohol. It is recommended not to drink alcohol during treatment with Flupentixol.

WARNINGS: *Neuroleptic Malignant Syndrome:* Neuroleptic malignant syndrome (NMS) is a rare, sometimes fatal, neurological disorder that

has been reported in association with antipsychotic drugs including Flupentixol. *Elderly Patients with Dementia:* Flupentixol is not indicated for the treatment of patients with dementia. *Adverse Reactions related to Drug Accumulation:* To lessen the likelihood of adverse reactions related to drug accumulation, patients on long-term therapy, particularly on high doses, should be evaluated periodically to decide whether the maintenance dosage can be lowered or drug therapy discontinued. *Anticholinergic Effects:* Although its anticholinergic properties are relatively weak, Flupentixol should be used with caution in patients who are known or are suspected to have glaucoma. Caution should also be taken in patients who might be exposed to extreme heat, or organophosphorus insecticides or who are receiving atropine or related drugs. Paralytic ileus has occasionally been reported, particularly in the elderly, when several drugs with anticholinergic effects have been used simultaneously. *Cardiotoxicity:* Flupentixol may cause QT prolongation. Therefore, Flupentixol should be used with caution in susceptible individuals (with hypokalemia, hypomagnesemia, or genetic predisposition) and in patients with a history of cardiovascular disorders e.g. QT prolongation, significant bradycardia (<50 beats per minute), a recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmia. *Cardiovascular Disease:* Caution should be used when using Flupentixol in patients with severe arteriosclerosis or in those who may have a propensity for development of defects in cardiac conduction. *Cerebrovascular Accidents:* An approximately 3-fold increased risk of cerebrovascular adverse events has been seen in randomized placebo controlled clinical trials in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. An increased risk cannot be excluded for other antipsychotics or other patient populations. Flupentixol is not indicated in patients with dementia. *Vascular Disease:* Flupentixol should be used with caution in patients with risk factors for stroke or with a history of stroke. *Venous Thromboembolism:* All possible risk factors for venous thromboembolism (VTE) should be identified before and during treatment with Flupentixol and preventive measures undertaken. *Cerebrovascular Adverse Events (CVAEs) including stroke in Elderly Patients with Dementia:* Flupentixol is not indicated in elderly patients with dementia. *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. *Non-teratogenic effects:* Neonates exposed to antipsychotic drugs (including Flupentixol) during the third trimester of pregnancy are at a risk for extrapyramidal and/or withdrawal symptoms following delivery.There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorder in these neonates. Flupentixol should not be administered to women of childbearing potential, unless, in the opinion of the physician, the expected benefit to the patient outweighs the potential risk to the fetus or child. *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. *Occupational Hazards/Sedative Effects:* Although Flupentixol is a relatively non-sedating drug, sedation may occur in some patients. Therefore, ambulatory patients should be warned about engaging in activities such as driving a car or operating machinery and about the concomitant use of alcohol and other CNS depressant drugs, since potentiation of their effects may occur. *Patients with Parkinson's Disease:* Flupentixol should be used with caution in patients with Parkinsonism, as it is known that dopamine antagonists such as Flupentixol, can cause a deterioration of the disease. *Seizures:* Flupentixol should be used with caution in patients with a history of convulsive disorders, as drugs of this class are known to lower seizure threshold. *Tardive Dyskinesia:* If the signs and symptoms of tardive dyskinesia develop during treatment with Flupentixol, withdrawal of the drug should be considered. *Hyperprolactinemia:* Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Long-standing hyperprolactinemia, when associated with hypogonadism, may lead to decreased bone mineral density in both female and male subjects. *Hyperglycemia:* Diabetic ketoacidosis (DKA) has occurred in patients with no reported history of hyperglycemia. Patients should have baseline and periodic monitoring of blood glucose and body weight. *Genitourinary:* Rare cases of priapism have been reported with antipsychotic use, such as Flupentixol. *Evaluation of Tolerance and Response:* The evaluation of tolerance and response, and establishment of adequate maintenance therapy require careful stabilization of each patient under continuous, close medical observation and supervision. *Hematologic:* Neutropenia, leukopenia, granulocytopenia and agranulocytosis have been reported during antipsychotic use, including with Flupentixol. *Hepatic/Biliary/Pancreatic/Renal:* Liver damage has been reported with this class of drugs. Therefore, hepatic function tests are advisable, particularly during the first months of therapy. *Ophthalmologic:* Although its anticholinergic effects are weak, Flupentixol use should be avoided in patients who are known to have, or suspected of having narrow angle glaucoma. *Photosensitivity Reactions:* Lens opacity has been reported rarely with Flupentixol. *Patients Undergoing Surgery:* Patients on large doses of Flupentixol who are undergoing surgery should be watched carefully for possible hypotensive phenomena and anesthetic or central nervous system depressant drug dosages may have to be reduced. *Sexual Function / Reproduction:* Adverse events such as hyperprolactinemia, galactorrhoea, amenorrhoea, decreased libido, erectile dysfunction and ejaculation failure have been reported in patients. These events may have a negative impact on female and/or male sexual function and fertility. *Antiemetic Effects:* The antiemetic effect observed with Flupentixol in animal studies may also occur in man; therefore, the drug may mask signs of toxicity due to overdosage of other drugs, or it may mask the symptoms of disease, such as brain tumor or intestinal obstruction.

DOSAGE & ADMINISTRATION: Flupenscot is administered by deep intramuscular injection into the gluteal region. Injection volumes exceeding 2 ml should be distributed between 2 injection sites. Local tolerability is good. Flupenscot is NOT for intravenous use. Dosage and interval between injections should be individually adjusted according to the therapeutic response. The onset of action usually occurs in the range of 24 to 72 hours after injection and the improvement of symptoms continues for 2 to 4 weeks. *Adults:* Recommended dose in adults is 20 to 40 mg by deep intramuscular injection and the interval between injections will usually be 2 to 4 weeks. *Elderly patients:* The use of Flupenscot 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. *Children:* Flupenscot is not recommended for children.

SPECIAL INSTRUCTIONS TO THE PHYSICIAN: 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.

STORAGE/PRECAUTIONS: Store in a cool, dry and dark place below 25 °C. Keep all medicines out of the reach of children. To be used on the prescription of Registered Medical Practitioners only.

PRESENTATION: Flupenscot 40 mg/ml Injection is available in a packing containing 1 ampoule.

عمومی خوراک: ڈاکٹر کی ہدایت کے مطابق۔ احتیاط: دوا صرف مستند ڈاکٹر کے زیر ہدایت استعمال کریں۔ روشنی، نمی اور گرمی سے بچائیں۔ 25 ڈگری سینٹی گریڈ سے کم درجہ حرارت پر محفوظ کریں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

Complete Medical Information available only for doctors on request.

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