



Fluanxol® Depot

Flupentixol decanoate (BP 1993: Flupentixol injection)

A POTENT NEUROLEPTIC FOR LONG-TERM THERAPY

COMPOSITION

Oily injection fluid: 1 ml contains 20 mg or 100 mg cis(Z)-flupentixol decanoate in thin vegetable oil intended for intramuscular injection.

PHARMACOLOGICAL INFORMATION

Pharmacological effects and mode of action

Fluanxol Depot is a thioxanthene derivative with pronounced antipsychotic, alerting and anxiolytic effects.

The antipsychotic effect of neuroleptics is normally related to their dopamine receptor blocking effect, which seems to release a chain reaction as other transmitter systems are influenced as well.

Fluanxol Depot is especially suitable for the treatment of chronic psychotic patients. The antipsychotic effect increases with increasing dosages. In low to moderate dosages (up to 100 mg/2 weeks) Fluanxol Depot is non-sedating, while an unspecific sedative effect may be anticipated when higher doses are administered. Fluanxol is relatively short-acting whereas Fluanxol Depot has a considerably prolonged duration of action.

Fluanxol Depot permits continuous antipsychotic treatment especially of those patients who are unreliable in taking the medication prescribed for them. Fluanxol Depot thus prevents the frequent relapses caused by failure to take oral medication.

Pharmacokinetics

Pharmacokinetic and clinical studies on Fluanxol Depot have shown that Fluanxol Depot injections can be given with intervals of 2 to 4 weeks. After injection cis(Z)-flupentixol decanoate undergoes enzymatic breakdown into the active component, cis(Z)-flupentixol and decanoic acid. Cis(Z)-flupentixol in small amounts crosses the placental barrier; cis(Z)-flupentixol is excreted in small amounts with the milk. The metabolites are devoid of neuroleptic activity. The excretion proceeds mainly with feces but also to some degree with the urine. The maximal serum concentration of cis(Z)-flupentixol is reached by the end of the first week after injection. The serum concentration curve declines exponentially with a half-life of approximately 3 weeks, reflecting the rate of release from the depot.

Pharmacokinetically a dose of 40 mg/2 weeks of Fluanxol Depot is equivalent to a daily oral dose of 10 mg Fluanxol.

CLINICAL INFORMATION

Indications

Schizophrenia and mania.

Contraindications

Hypersensitivity to Fluanxol or other thioxanthenes. Acute alcohol, barbiturate, and opiate intoxications; comatose or CNS depressed states. Not recommended for excitable or overactive patients since its activating effect may lead to exaggeration of these characteristics. Do not use in senile confusional states.

Adverse effects

Neurological: Extrapyramidal symptoms may occur, especially during the early phase of treatment. In most cases these side effects can be satisfactorily controlled by reduction of dosage and/or antiparkinsonian drugs. The routine prophylactic use of antiparkinsonian medication is not recommended. Tardive dyskinesias may occur very occasionally in patients on long-term therapy. Antiparkinsonian drugs do not alleviate these symptoms. Reduction in dosage or, if possible, discontinuation of therapy is recommended.

Psychic: Transient insomnia, especially when the patient is switched over from sedative neuroleptics. At high dosage a sedative effect may occur in the occasional patient.

Autonomic and cardiovascular: Very rare in the therapeutic dosage range. **Liver:** Transient slight alterations in liver function tests may occur.

Fluanxol, even in low doses, in susceptible (especially non-psychotic) individuals may unusually cause nausea, dizziness or headache, excitement, agitation, insomnia, or unpleasant subjective feelings of being mentally dulled or slowed down.

Epileptic fits have occasionally been reported. Confusional states can occur.

The hormonal effects of antipsychotic neuroleptic drugs include hyperprolactinaemia, which may be associated with galactorrhoea, gynaecomastia, oligomenorrhoea or amenorrhoea. Sexual function, including erection and ejaculation may rarely be impaired; but increased libido has also been reported.

Weight gain and less commonly weight loss have been reported; oedema has occasionally been reported and has been considered to be allergic in origin. Rashes have occurred rarely. Although less likely than with phenothiazines, flupentixol can rarely cause increased susceptibility to sunburn.

ECG changes with prolongation of the QT interval and T-wave changes may occur with moderate to high doses; they are reversible on reducing the dose.

Flupentixol may impair body temperature control, and cases of hyperthermia have occurred rarely. The possible development of hypothermia, particularly in the elderly and hypothyroid, should be borne in mind. Because acute withdrawal symptoms, including nausea, vomiting and insomnia have very rarely been described after abrupt cessation of high doses of phenothiazines, gradual withdrawal of flupentixol is advisable. Blood dyscrasias have occasionally been reported. Blood counts should be carried out if a patient develops signs of persistent infection. Jaundice and other liver abnormalities have been reported rarely, but have never been confirmed to be flupentixol-induced.

Precautions

Fluanxol Depot should be used with caution in patients with convulsive disorders or advanced hepatic, cardiovascular, renal, or severe respiratory disease, Parkinson, myasthenia gravis, phaeochromocytoma, narrow angle glaucoma, prostatic hypertrophy, or hypothyroidism. If the patient has been treated previously with neuroleptics with sedative effect, these should be withdrawn gradually. Patients on long-term therapy particularly on high doses should be monitored carefully and evaluated periodically to decide whether the maintenance dosage can be lowered.

Use during pregnancy and lactation

Fluanxol Depot should preferably not be given during pregnancy and lactation.

Drug interactions

Fluanxol Depot may enhance the response to alcohol and the effects of barbiturates and other CNS depressants. Fluanxol Depot should not be given concomitantly with guanethidine or similar acting compounds, since neuroleptics may block the antihypertensive effect of these compounds. Fluanxol Depot may lower the effect of levodopa and

adrenergic drugs and concomitant use of metoclopramide and piperazine increases the risk of extrapyramidal symptoms.

Flupentixol weakly antagonises the action of adrenaline and other sympathomimetic agents and may reverse the blood pressure lowering effects of adrenergic blocking agents, such as guanethidine, possibly also clonidine.

It may possibly affect the control of diabetes or the action of anticoagulants.

Phenothiazines may enhance the cardiac depressant effect of quinidine, the absorption of corticosteroids and digoxin, the effect of diazoxide and neuromuscular blocking agents.

Dosage regimen

Adults:

Fluanxol Depot is administered by intramuscular injection into the upper outer quadrant of the buttock. Local tolerability is good. Dosage and interval between injections should be individually adjusted according to the therapeutic response.

Fluanxol Depot 20 mg/ml: In the maintenance treatment the dosage range would normally be 20-40 mg (1-2 ml) every 2-4 weeks.

A few patients may need higher doses or shorter intervals between doses.

If volumes larger than 2-3 ml of the 20 mg/ml solution are required the more concentrated solution (Fluanxol Depot 100 mg/ml) should be preferred.

If volumes greater than 2 ml are used, the injection should be distributed between two injection sites.

Fluanxol Depot 100 mg/ml: 50-200 mg (1/2-2 ml) every 2-4 weeks.

During an exacerbation or acute relapse of the illness, single injections of as much as 400 mg fortnightly, or even weekly, may be required.

As soon as adequate control of symptoms has been achieved, gradual decrease is made to a suitable maintenance dose, usually in the range 20-200 mg every 2-4 weeks.

When changing the medication from oral Fluanxol to maintenance treatment with Fluanxol Depot the following guideline should be used: x mg Fluanxol orally daily x 4 = x mg Fluanxol Depot i.m. every second week.

Oral Fluanxol should be continued during the first week after the first injection but in diminishing dosage. Subsequent doses and intervals between injections should be adjusted according to the patient's response. Reduced doses are recommended for the elderly or debilitated patients.

Overdose

Symptoms:

Somnolence, coma, extrapyramidal symptoms, convulsions, hypotension, shock, hyper- or hypothermia.

Treatment:

Symptomatic and supportive. Measures aimed at supporting the respiratory and cardiovascular systems should be instituted.

Epinephrine (adrenaline) should not be used, as further lowering of blood pressure may result. Convulsions may be treated with diazepam and extrapyramidal symptoms with biperiden.

Special warnings

The neuroleptic malignant syndrome (NMS) is a rare but potentially fatal complication of the use of neuroleptic drugs. Core features of NMS are hyperthermia, muscular rigidity and fluctuating consciousness along with autonomic dysfunction (labile blood pressure, tachycardia, diaphoresis).

Aside from immediate cessation of the neuroleptic medication, the use of general supportive measures and symptomatic treatment are vital.

Warning

Effects on ability to drive or operate machinery.

Although Fluanxol Depot is a non-sedating drug the ability to drive or operate machinery may be affected. Drowsiness and sedation are unusual. Sedation, if it occurs, is more often seen with high dosage and at the start of treatment, particularly in the elderly. Therefore, caution should be exercised initially, until the individual's reaction to treatment is known. Other adverse effects include blurring of vision, tachycardia and urinary incontinence and frequency. Dose-related postural hypotension may occur, particularly in the elderly.

PHARMACEUTICAL INFORMATION

Incompatibilities

Fluanxol Depot should not be mixed with other injection fluids.

Dosage form/Description of product

Fluanxol Depot 20 mg/ml

Fluanxol Depot 100 mg/ml

A clear yellowish oil

Storage conditions and shelf life

Fluanxol Depot is valid for 4 years when stored at max 25°C, protected from light.

Each pack has open expiry date.

Keep out of reach of children.

Packs

Glass ampoules in carton.

Fluanxol Depot 20 mg/ml:

Ampoules of 1 ml (20 mg)

Ampoules of 2 ml (40 mg)

Fluanxol Depot 100 mg/ml:

Ampoules of 1 ml (100 mg)

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