Fluphenazine Decanoate Injection, USP

PACKAGE INSERT

FLUPHENAZINE DECANOATE INJECTION, USP
25 mg/mL
Rx Only

DESCRIPTION

Fluphenazine decanoate is the decanoate ester of a trifluoromethyl phenothiazine derivative. Fluphenazine Decanoate is C₂₅H₂₇ClF₂N₂O₄S, an oil in a sesame oil vehicle with 1.2% (w/v) benzyl alcohol as a preservative. Fluphenazine decanoate has the following structural formula:

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\text{C}_{25}\text{H}_{27}\text{ClF}_{2}\text{N}_{2}\text{O}_{4}\text{S}
\]

591.8

CLINICAL PHARMACOLOGY

The basic effects of fluphenazine decanoate appear to be no different from those of fluphenazine hydrochloride, with the exception of duration of action. The esterification of fluphenazine markedly prolongs the drug’s duration of effect without unduly attenuating its beneficial action.

Fluphenazine decanoate has activity at all levels of the central nervous system as well as on multiple organ systems. The mechanism whereby its therapeutic action is exerted is unknown.

Fluphenazine differs from other phenothiazine derivatives in several respects: It is more potent on a milligram basis; it has less potentializing effect on central nervous system depressants and anesthetics than do some of the phenothiazines and appears to be less sedating, and it is less likely than some of the older phenothiazines to produce hypotension (nevertheless, appropriate cautions should be observed – see sections on PRECAUTIONS and ADVERSE REACTIONS).

INDICATIONS AND USAGE

Fluphenazine Decanoate Injection is a long-acting parenteral antipsychotic drug intended for use in the management of patients requiring prolonged parenteral neuroleptic therapy (e.g., chronic schizophrenia).

Fluphenazine Decanoate Injection has not been shown effective in patients with organic brain syndromes or in patients with comatose or severely depressed states. The presence of blood dyscrasia or liver damage precludes the use of fluphenazine decanoate.

Fluphenazine Decanoate Injection is contraindicated in comatose or severely depressed states. Fluphenazine Decanoate Injection is contraindicated in patients with a previously documented intolerance to fluphenazine. Fluphenazine Decanoate Injection should be used cautiously in patients who have ingested large quantities of alcohol or who have a history of alcoholism or hepatic abnormalities.

Usage in Pregnancy:

The safety for the use of this drug during pregnancy has not been established; therefore, the possible hazards should be weighed against the potential benefits when administering this drug to pregnant patients.

PRECAUTIONS

General:

Because of the possibility of cross-sensitivity, fluphenazine decanoate should be used cautiously in patients who have developed cholestatic jaundice, dermatoses, or other allergic reactions to phenothiazine derivatives.

Psychotic patients on large doses of a phenothiazine drug who are undergoing surgery should be watched carefully for possible hypotensive phenomena. Moreover, it should be remembered that reduced amounts of anesthetics or central nervous system depressants may be necessary.

The effects of atropine may be potentiated in some patients receiving fluphenazine because of added anticholinergic effects.

Fluphenazine decanoate should be used cautiously in patients exposed to extreme heat or phosphorus insecticides.

The preparation should be used with caution in patients with a history of convulsive disorders, since grand mal convulsions have been known to occur.

Use with caution in patients with special medical disorders such as mitral insufficiency or other cardiovascular diseases and pheochromocytoma.

The possibility of liver damage, pigmentary retinopathy, lenticular and corneal deposits, and development of irreversible dyskinesia should be remembered when patients are on prolonged therapy. Outside state hospitals or other psychiatric institutions, fluphenazine decanoate should be administered under the direction of a physician experienced in the clinical use of psychotropic drugs, particularly phenothiazine derivatives.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias).

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., sepsis, diabetic ketoacidosis, and unexplained fever) or inadequately treated extrapyramidal symptoms and signs (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

The use of this drug may impair the mental and physical abilities required for driving a car or operating heavy machinery.

Physicians should be alert to the possibility that severe adverse reactions may occur which require immediate medical attention.

Potentiation of the effects of alcohol may occur with the use of this drug.

Since there is no adequate experience in pediatric patients who have received this drug, safety and efficacy in pediatric patients have not been established.

ADVERSE REACTIONS

Central Nervous System:

The side effects most frequently reported with phenothiazine compounds are extrapyramidal symptoms including pseudoparkinsonism, dystonia, dyskinesia, akathisia, oculogyric crises, ophthalmoparesis, and hyperreflexia. Muscle rigidity sometimes accompanies the previously reported following use of fluphenazine decanoate. Most often these extrapyramidal symptoms are reversible; however, they may be persistent (see below). The frequency of such reactions is related in part to chemical structure.
Hematologic: Routine blood counts are advisable during therapy since blood dyscrasias including leukopenia, agranulocytosis, thrombocytopenic or normoblastic anemia, purpura, eosinophilia, and pancytopenia have been observed with phenothiazine derivatives. Furthermore, if any soreness of the mouth, gums, or throat, or any symptoms of upper respiratory infection occur and confirmatory leukocyte count indicates cellular depression, therapy should be discontinued and other appropriate measures instituted immediately.

Hepatic: Liver damage as manifested by cholestatic jaundice may be encountered, particularly during the first months of therapy; treatment should be discontinued if this occurs. An increase in cephalin flocculation, sometimes accompanied by alterations in other liver function tests, has been reported in patients receiving the erasable ester of fluphenazine (a closely related compound) who have had no clinical evidence of liver damage.

Others: Sudden, unexpected and unexplained deaths have been reported in hospitalized psychotic patients receiving phenothiazines. Previous brain damage or seizures may be predisposing factors; high doses should be avoided in known seizure patients. Several patients have shown sudden flare-ups of psychotic behavior patterns shortly before death. Autopsy findings have usually revealed acute fulminating pneumonia or pneumonitis, aspiration of gastric contents, or intramyocardial lesions.

Although this is not a general feature of fluphenazine, potentiation of central nervous system depressants (opiates, analgesics, anesthetic’s, barbiturates, alcohol) may occur.

The following adverse reactions have also occurred with phenothiazine derivatives: systemic lupus erythematosus-like syndrome, hypotension severe enough to cause fatal cardiac arrest, altered electrocardiographic and electroencephalographic tracings, altered cerebrospinal fluid proteins, cerebral edema, asthma, laryngeal edema, and angioneurotic edema; with long-term use—skin pigmentation, and lenticon and cecometic opalescences.

DOSAGE AND ADMINISTRATION

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Fluphenazine Decanoate Injection may be given intramuscularly or subcutaneously. A dry syringe and needle of at least 21 gauge should be used. Use of a wet needle or syringe may cause the solution to become cloudy.

To begin therapy with Fluphenazine Decanoate Injection the following regimens are suggested:

For most patients, a dose of 12.5 to 25 mg (0.5 to 1 mL) may be given to initiate therapy. The onset of action generally appears between 24 and 72 hours after injection and the effects of the drug on psychotic symptoms becomes significant within 48 to 96 hours. Subsequent injections and the dosage interval are determined in accordance with the patient’s response. When administered as maintenance therapy, a single injection may be effective in controlling schizophrenic symptoms up to four weeks or longer. The response to a single dose has been found to last as long as six weeks in a few patients on maintenance therapy.

It may be advisable to patients who have no history of taking phenothiazines should be treated initially with a shorter-acting form of fluphenazine before administering the decanoate to determine the patient’s response to fluphenazine and to establish appropriate dosage. For psychotic patients who have been stabilized on a fixed daily dosage of Fluphenazine Hydrochloride Tablets, Fluphenazine Hydrochloride Elux, or Fluphenazine Hydrochloride Oral Solution, conversion of therapy from these short-acting oral forms to the long-acting Fluphenazine Decanoate Injection may be indicated.

Appropriate dosage of Fluphenazine Decanoate Injection should be individualized for each patient and responses carefully monitored. No precise formula can be given to convert to use of Fluphenazine Decanoate Injection; however, a controlled multicentered study*, in patients receiving oral doses from 5 to 60 mg Fluphenazine hydrochloride daily, showed that 20 mg fluphenazine hydrochloride daily was equivalent to 25 mg (1 mL) Fluphenazine Decanoate Injection. This represents an approximate conversion ratio of 0.5 mL (12.5 mg) of decanoate every three weeks for every 10 mg of fluphenazine hydrochloride daily.

Once conversion to Fluphenazine Decanoate Injection is made, careful clinical monitoring of the patient and appropriate dosage adjustment should be made at the time of each injection.

Severely agitated patients may be treated initially with a rapid-acting phenothiazine compound such as Fluphenazine Hydrochloride injection—see package insert accompanying that product for complete information. When acute symptoms have subsided, 25 mg (1 mL) of Fluphenazine Decanoate Injection may be administered; subsequent dosage is adjusted as necessary.

Allergic Reactions: Allergic reactions to phenothiazine derivatives have been known to occur in some patients on maintenance therapy, restlessness, excitement, or bizarre dreams.

Autonomic Nervous System: Autonomic reactions including nausea and loss of appetite, salivation, polyuria, perspiration, dry mouth, headache, and further lowering of blood pressure should not occur, supportive measures including the use of epinephrine should not be used. Use of a wet needle or syringe may cause the solution to become cloudy.

In some patients, phenothiazine derivatives have caused blurred vision, glaucoma, bladder paralysis, fecal impaction, paralytic ileus, tachycardia, or nasal congestion.

Metabolic and Endocrine: Weight change, peripheral edema, abnormal lactation, gynecomastia, menstrual irregularities, false results on pregnancy tests, impotence in men and increased libido in women have all been known to occur in some patients on phenothiazine therapy.

Allergic Reactions: Skin disorders such as itching, erythema, urticaria, seborrhea, photosensitivity, eczema and even exfoliative dermatitis have been reported with phenothiazine derivatives. The possibility of anaphylactoid reactions occurring in some patients should be borne in mind.

* The Initiation of Long-Term Pharmacotherapy in Schizophrenia: Dosage and Side Effect Comparisons Between Oral and Depot Fluphenazine; N.R. Schooler; Pharmakopsych. 9: 159-169, 1976.