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., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary CNS pathology.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent medical 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 that treatment with anticholinergic agents is helpful in 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.

Fluphenazine Decanoate Injection may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls and, consequently, fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating antipsychotic treatment and recurrently for patients on long-term antipsychotic therapy.

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 children who have received this drug, safety and efficacy in children have not been established.

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.

Use with caution in patients with special medical disorders such as mitral insufficiency or other cardiovascular disorders, chronic obstructive pulmonary disease, and diabetes mellitus.

The possibility of liver damage, pigmentary retinopathy, lunacular and corneal deposits, and development of irreversible dyskinesia should be remembered when patients are on prolonged therapy.

As with any antipsychotic, the physician should be alert to the possible development of “silent pneumonias” in patients under treatment with fluphenazine decanoate.

Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vivo, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs at all doses are at increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients and symptom-negative patients ranged from 0.5 to 0.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with classic antipsychotic drugs including haloperidol resulted in a higher risk of death compared with placebo at all levels of the central nervous system (CNS) as well as on multiple organ systems. The mechanism whereby its therapeutic action is exerted is unknown.

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

Fluphenazine decanoate injection is not approved for the treatment of patients with dementia-related psychosis (see BOXED WARNING).

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).

Central Nervous System

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

Leukopenia, Neutropenia and Agranulocytosis

Leukopenia, neutropenia, and agranulocytosis have been reported temporally related to antipsychotic agents.

Leukopenia, Neutropenia and Agranulocytosis

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To report SUSPECTED ADVERSE REACTIONS, contact Par Pharmaceutical at 1-800-828-9393 or FDA at 1-800-FDA-1088. The following adverse reactions have also occurred with phenothiazine derivatives: Systemic lupus erythematosus—antihistamines, barbiturates, alcohol may occur. Although this is not a general feature of fluphenazine, potentiation of CNS depressants (opiates, analgesics, death. Autopsy findings have usually revealed acute fulminating pneumonia or pneumonitis, aspiration of gastric phenothiazines. Previous brain damage or seizures may be predisposing factors; high doses should be avoided in some patients should be borne in mind.

**Allergic Reactions**

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

**Metabolic and Endocrine**

Skin disorders including xerosis, erythema, urticaria, seborrhea, photosensitivity, eczema and exfoliative dermatitis have been reported with phenothiazine derivatives. The possibility of anaphylactoid reactions occurring in some patients should be borne in mind.

**Hematologic**

Routine blood counts are advisable during therapy since blood dyscrasias including leukopenia, agranulocytosis, thrombocytopenia or nonthrombocytopenic purpura, eosinophilia, and pancytopenia have been observed with phenothiazine derivatives. With closely when the drug is administered. If severe hypotension should occur, supportive measures including the use of pressor vasopressor drugs should be instituted immediately. Norepinephrine Bitartrate Injection is the most suitable drug for this purpose. Metoclopramide should not be used since phenothiazine derivatives have been found to reverse its action, resulting in a further lowering of blood pressure.

**Autonomic Reactions** including nausea and loss of appetite, salivation, polyuria, perspiration, dry mouth, headache, constipation may occur. Autonomic effects can usually be controlled by reducing or temporarily discontinuing dosage.

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

**WARNINGS**

**Hypertension**

Hypertension has rarely presented a problem with fluphenazine. However, patients with pheochromocytoma, cerebral, vascular or renal insufficiency, or a severe cardiac reserve deficiency such as mitral insufficiency appear to be particularly prone to hypertension reactions with phenothiazine compounds, and should therefore receive them only with caution. Additionally,Exclude patients with known hypersensitivity to phenothiazines, or with disorders that predispose to undue hypotension. Therapy may be initiated cautiously with oral or parenteral fluphenazine hydrochloride (see Package Inserts accompanying this 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. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

**HOW SUPPLIED**

Fluphenazine Decanoate Injection, USP NDC 40212-115-01: 25 mg/mL in 5 mL multiple dose, flip-top vial individually packaged. Store at 20° to 25°C (68° to 77°F) (see USP Controlled Room Temperature). Protect from light. Retain vial in carton until ready for use. Vial stoppers do not contain natural rubber latex.

**Rx Only**


R11/16 3003346B

For more information, contact Par Pharmaceutical at 1-800-828-9393 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DOSAGE AND ADMINISTRATION**

Fluphenazine Decanoate Injection may be given IM or SC. 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 patients who may be advised that 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, USP or Fluphenazine Hydrochloride Elavil, USP conversion of therapy from these short-acting oral forms to the long-acting Fluphenazine Decanoate Injection may be indicated.**