FLUDECATE
FOR INTRAMUSCULAR INJECTION

Fludecate (Fluphenazine Decanoate) is the decanoate ester of the potent neuroleptic Fluphenazine. The Fluphenazine Decanoate is slowly absorbed from the intramuscular site of injection and is then hydrolysed in the plasma to the active therapeutic agent.

Fludecate is a highly potent behavior modifier with a markedly extended duration of effect.

Clinical Pharmacology:

Fluphenazine decanoate has activity 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 differs from other phenothiazine derivatives in several respects: it is more potent on a milligram basis, it has less potentiating effect on CNS 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 PRECAUTIONS and ADVERSE REACTIONS).

Composition: Each ampoule of 1ml. contains: Fluphenazine decanoate B.P. 25mg. Fludecate is an oily preparation for intramuscular injection, in Sesame oil solution. It contains also 1.5 % Benzyl alcohol as preservative.

Indications: Fludecate is a is a long acting parenteral antipsychotic drug intended for use in the management of patients requiring prolonged parenteral neuroleptic therapy (e.g., chronic schizophrenics).

Fluphenazine Decanoate Injection has not been shown effective in the management of behavioral complications in patients with mental retardation.

Dosage and directions for use:

For most patients a dose of 12.5 mg to 25 mg (0.5 ml to 1 ml) may be given to initiate treatment (For patients of/over 60 years of age a dose of 0.25 ml is recommended to initiate treatment).
Clinical response or side effects may be observed within hours

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 dosage interval are determined in accordance with the patient's response and severity of condition. 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.

Elderly:

Elderly patients may be particularly susceptible to extrapyramidal reactions, sedative and hypotensive effects. In order to avoid this, a reduced maintenance dosage may be required and a smaller initial dose (see above).

It may be advisable that patients who have had no history of taking phenothiazines should be treated initially with Fluphenazine tablets (Selecten).

The optimal amount of the drug and the frequency of administration must be determined for each patient, since dosage requirements have been found to vary with clinical circumstances as well as with individual response to the drug.

Dosage should not exceed 100 mg. If doses greater than 50 mg are deemed necessary, the next dose and succeeding doses should be increased cautiously in increments of 12.5 mg.

Fludecate is administered by deep intramuscular injection into the gluteal region 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. Fludecate is not intended for use in children under 12 years of age.

It is preferable that patients be stabilised on the injection in hospital. Fludecate is a hospital follow up drug.

Contraindications:
Phenothiazines are contraindicated in patients with suspected or established subcortical brain damage. Phenothiazine compounds should not be used in patients receiving large doses of hypnotics. Fludecate is contraindicated in comatose or severely depressed states and in severe cardiovascular diseases. The presence of blood or liver damage precludes the use of Fluphenazine decanoate. Fluphenazine decanoate is not intended for use in children under 12 years of age. Since Fludecate
contains Benzyl alcohol it should not be used in prematures and neonates. Fluphenazine Decanoate injection is contraindicated in patients who have shown hypersensitivity to fluphenazine, cross-sensitivity to phenothiazine derivatives may occur.

Warnings:
Increased Mortality in Elderly Patients with Dementia-Related Psychosis: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an 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 between 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 was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most deaths appeared to be either cardiovascular (CV) (e.g., heart failure, sudden death)

or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patient is not clear.

Fluphenazine decanoate is not approved for the treatment of patients with dementia-related psychosis.

Tardive Dyskinesia:

Tardive Dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with neuroleptic (antipsychotic) drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if neuroleptic treatment is withdrawn.

Neuroleptic treatment, itself, however may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, neuroleptics should be prescribed in a manner that is most likely to minimize the occupance of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that 1) known to respond to neuroleptic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be reassessed periodically. If signs and symptoms of tardive dyskinesia appears in a patient on neuroleptics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

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 automatic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). The diagnostic evaluation of patients with this syndrome is complicated. In

arriving at the 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. Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system pathology. The management of NMS should include: 1) immediate discontinuation of antipsychotic 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 pharmacologic 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 children who have received this drug, safety and efficacy in children have not been established.
Fluphenazine decanoate is not intended for use in children under 12 years of age

- The use of Fludecate during Lactation should be avoided.

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:

Leukopenia, Neutropenia and Agranulocytosis

In clinical trial and postmarketing experience, events of leukopenia/neutropenia and agranulocytosis have been reported temporally related to antipsychotic agents.

Possible risk factors for leukopenia/neutropenia include preexisting low white blood cell count (WBC) and history of drug induced leukopenia/neutropenia. Patients with a preexisting low WBC or a history of drug induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and should discontinue Fludecate at the first sign of a decline in WBC in the absence of other causative factors.

Patients with neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or

signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm^3) should discontinue Fludecate and have their WBC followed until recovery.

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 decanoate 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 pheochoromocytoma.

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.

Fluphenazine Decanoate should be administered under the direction of a physician experienced in the clinical use of psychotropic drugs, particularly phenothiazine derivatives. Furthermore, facilities should be available for periodic checking of hepatic function, renal function, and the blood picture. Renal function of patients on long-term therapy should be monitored, if BUN (blood urea nitrogen) becomes abnormal, treatment should be discontinued.

As with any phenothiazine, 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 vitro, 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.

Information for Patients

Given the likelihood that a substantial proportion of patients exposed chronically to neuroleptics will develop tardive dyskinesia, it is advised that all patients in whom chronic use is contemplated be given, if possible, full information about this risk. The decision to inform patients and/or their guardians must obviously take into account the clinical circumstances and the competency of the patient to understand the information provided.

Pregnancy Non-teratogenic Effects
Neonates exposed to antipsychotic drugs, during the third trimester of pregnancy are at 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. These complications have varied in severity; while in some cases symptoms have been self limited, in other cases neonates have required intensive care unit support and prolonged hospitalization.

Fludecate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Drug interactions:
drug Interactions with major clinical significance:
• ***Alcohol or other CNS depressants -*** concurrent use with phenothiazines may result in increased CNS and respiratory depression and increased hypotensive effects, dosage reductions of either drug may be necessary during concurrent use or when sequence of use enhances CNS effects, alcohol may increase the risk of heat stroke when taken concurrently with phenothiazines. The possibility should be borne on mind that phenothiazines may increase the central nervous system depression produced by drugs such as alcohol, general anaesthetics, hypnotics, sedatives or strong analgesics.
• ***Tricyclic antidepressant or Monoamine oxidase (MAO) inhibitors, including furazolidone, procarbazine, and selegiline -*** concurrent use may prolong and intensify the sedative and anticholinergic effects of either these medications or phenothiazines: phenothiazines may increase plasma concentrations of cyclic antidepressants and may inhibit phenothiazine metabolism, also the risk of neuroleptic malignant syndrome [NMS] may be increased.
• ***Antithyroid agents -*** concurrent use with phenothiazines may increase the risk of agranulocytosis.
• ***Epinephrine*** - the use of epinephrine to treat phenothiazine induced hypotension should be avoided because the alpha-adrenergic effects of epinephrine may be blocked, resulting in beta stimulation only and causing severe hypotension and tachycardia.
• ***Medications causing extrapyramidal reaction -*** concurrent use with phenothiazines may increase the severity and frequency of extrapyramidal effects.
• ***Medication producing hypotension -*** concurrent use with phenothiazines may produce sever hypotension with postural syncope.
• ***Levodopa -*** antiparkinsonian effects of levodopa may be inhibited when it is used concurrently with phenothiazines, because of blockade of dopamine receptors in brain, levodopa has not been shown to be effective in the treatment of phenothiazine-induced parkinsonism.

• ***Metrizamide*** – concurrent use with phenothiazines may lower the seizure threshold, phenothiazines should be discontinued at least 48 hours before, and not resumed for at least 24 hours following, myelography.
• ***Lithium*** - concurrent use with chlorpromazine and possibly other phenothiazines may reduce gastrointestinal absorption of the phenothiazine, thereby decreasing its serum concentrations by as much as 40%. Concurrent use may increase rate or renal excretion of lithium, extrapyramidal symptoms may be increased, also, nausea and vomiting, early indications of lithium toxicity, may be masked by the antiemetic effect of some phenothiazines.
• ***Amantadine, antidyskinetics, antihistamines, anticholinergic or other medications with anticholinergic action -*** concurrent use with phenothiazines may intensify anticholinergic side effects, especially confusion, hallucinations, and nightmares, because of the phenothiazines secondary anticholinergic effects, medications with anticholinergic effects may potentiate the hyperpyretic effect of phenothiazines, especially when environmental temperatures are high, by preventing sweating as a cooling mechanism; this effect could lead to heat stroke; also, patients should be advised to report occurrence of gastrointestinal problems since paralytic ileus may occur with concurrent therapy. Trihexyphenidyl may decrease. plasma phenothiazine concentrations by decreasing gastrointestinal motility and increasing metabolism of the phenothiazine. Since the antipsychotic effectiveness may be reduced, dosage adjustment of the phenothiazine may be required. Parental methotrimeprazine, used as preanesthetic medication, administered concurrently, but with caution, with lowered doses of atropine or scopolamine: tachycardia and a fall in blood pressure may occur, and CNS reaction, such as stimulation, delirium, and extrapyramidal reactions, may be aggravated.
• **Amphetamines -** stimulant effects may be decreased when amphetamines are used concurrently with phenothiazines since phenothiazines produce alpha-adrenergic blockade, also, the antipsychotic effectiveness of phenothiazines may be reduced.
• ***Antacids, (containing aluminum – or magnesium), antidiarrheals (absorbent)*** - concurrent use of these medications with phenothiazines may inhibit the absorption of orally administered phenothiazines (especially chlorpromazine), simultaneous use should be avoided.
• **Anticonvulsants, including barbiturates -** phenothiazines may lower the seizure threshold: dosage adjustment of anticonvulsant medications may be necessary. Phenothiazines may inhibit phenytoin metabolism, leading to phenytoin toxicity.
• ***Apomorphine.-*** prior ingestion of phenothiazine antiemetics may decrease the emetic response to apomorphine, also the CNS depressant effect of phenothiazine antiemetics are additive to those of apomorphine and may induce dangerous respiratory depression, circulatory system effects, or prolonged sleep.
• ***Appetite suppressants –*** concurrent use with phenothiazines may antagonize the anorectic effect of appetite suppressants, with the exception of fenfluramine and phenmetrazine.
• ***Beta-adrenergic blocking agents -*** concurrent use of beta-blockers, possibly including ophthalmics, with phenothiazines may result in an

increased plasma concentration of each medication because of inhibition of metabolism; this may result in additive hypotension effects, irreversible retinopathy, cardiac arrhythmias, and tardive dyskinesia.
• **Bromocriptine -** concurrent use may increase serum prolactin concentrations and interfere with effects of bromocriptine. Dosage adjustment may be necessary.
• ***Thiazide diuretics -*** concurrent use may potentiate hyponatremia and water intoxication; alternate methods of hypertension control should be considered.
• ***Dopamine*** - concurrent use may antagonize the peripheral vasoconstriction produced by high doses of dopamine.
• ***Ephedrine*** - concurrent use may decrease the pressor response to ephedrine.
• ***Hepatotoxic medications*** - concurrent use of phenothiazines with medications known to alter hepatic microsomal enzyme activity may result in an increased incidence of hepatotoxicity; patients, especially those on prolonged administration or with a history of liver disease, should be carefully monitored.
• ***Metaraminol*** – concurrent use with phenothiazines usually decreases, but dose not reverse or completely block, the pressor effect of metaraminol because of the alpha-adrenergic blocking action of phenothiazines.
• ***Mephentermine*** - concurrent use with phenothiazines, especially chlorpromazine, may antagonize the antipsychotic effect of the phenothiazine or the pressor effect of mephentermine by exerting opposing effects on monoaminergic functions in the central and peripheral nervous system.
• ***Methoxamine*** – prior administration of phenothiazines may decrease the pressor effect and shorten the duration of action of methoxamine, because of the alpha-adrenergic blocking action of phenothiazines.
• ***Ototoxic medications, especially ototoxic antibiotics*** - concurrent use with phenothiazines may mask some symptoms of ototoxicity such as tinnitus, dizziness, or vertigo.
• ***Opioid (narcotic) analgestics in addition to increased CNS and respiratory depression-*** concurrent use with phenothiazines increases orthostatic hypotension and the risk of severe constipation, which may lead to paralytic ileus and/or urinary retention.
• ***Phenylephrine*** -prior administration of phenothiazines may decrease the pressor affect and shorten the duration of action of phenothiazine.
• ***Photosensitizing medications*** - concurrent use with phenothiazines may cause additive photosensitizing effects. In addition, concurrent use of systemic methoxsalen, trioxsaien or tetracyclines with phenothiazine may potentiate intraocular photochemical damage to the choroids, retina or lens.
• ***Probucol*** - additive QT interval prolongation may increase the risk of ventricular tachycardia.

Side effects:
Central Nervous System –
The side effects most frequently reported with phenothiazine compounds are extrapyramidal symptoms including pseudoparkinsonism, dystonia, dyskinesia, akathisia, oculogyric crises, opisthotonos, and hyperreflexia.

Muscle rigidity sometimes accompanied by hyperthermia has been 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: one can expect a higher incidence with fluphenazine decanoate than with less potent piperazine derivatives or with straight-chain phenothiazines such as chlorpromazine. With any given phenothiazine derivative, the incidence and severity of such reactions depend more on individual patient sensitivity than on other factors, but dosage level and patient age are also determinants.

Extrapyramidal reactions may be alarming, and the patient should be forewarned and reassured. These reactions can usually be controlled by administration of antiparkinsonian drugs such as Benztropine Mesylate or intravenous Caffeine and Sodium Benzoate Injection, and by subsequent reduction in dosage.

Dystonia - Class effect
Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic drugs. An elevated risk of acute dystonia is observed in males and younger age groups.

Tardive Dyskinesia
(see "Warnings") - The syndrome is characterized by involuntary choreoathetoid movements which variously involve the tongue, face, mouth, lips, or jaw (e.g., protrusion of the tongue, puffing of the cheeks, puckering of the mouth, chewing movements), trunk and extremities. The severity of the syndrome and the degree of impairment produced vary widely.

The syndrome may become clinically recognizable either during treatment, upon dosage reduction, or upon withdrawal of treatment. Early detection of tardive dyskinesia is important. To increase the likelihood of detecting the syndrome at the earliest possible time, the dosage of neuroleptic drug should be reduced periodically (if clinically possible) and the patient observed for signs of the disorder. This maneuver is critical, since neuroleptic drugs may mask the signs of the syndrome.

Other CNS effects
Occurrences of neuroleptic malignant syndrome (NMS) have been reported in patients on neuroleptic therapy (see Warnings, Neuroleptic Malignant syndrome).Leukocytosis, elevated CPK, liver function abnormalities and acute renal failure may also occur with NMS.

Drowsiness or lethargy, if they occur, may necessitate a reduction in dosage; the induction of a catatonic-like state has been known to occur with dosages of fluphenazine far in excess of the recommended amounts. As with other phenothiazine compounds, reactivation or aggravation of psychotic processes may be encountered.

Phenothiazines derivatives have been known to cause, in some patients, restlessness, excitement. or bizarre dreams**.**

Autonomic Nervous System –
Hypertension and fluctuations in blood pressure have been reported with fluphenazine.

Hypotension 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 hypotensive reactions with phenothiazine compounds, and should therefore be observed closely when the drug is administered. If severe hypotension should occur, supportive measures including the use of intravenous vasopressor drugs should be instituted immediately. Norepinephrine Bitartrate Injection is the most suitable drug for this purpose, epinephrine 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, and 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.

Metabolic and Endocrine –
weight changes, peripheral edema, gynecomastia, menstrual irregularities, false results on pregnancy tests, impotency 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.

Hematologic –
routine blood counts are advisable during therapy since blood dyscrasias including leukopenia, agranulocytosis, thrombocytopenic or nonthrombocytopenic 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 countered, 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 fluphenazine 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, antihistamines, 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 electroencephaiographic tracings, altered cerebrospinal fluid proteins, cerebral edema, asthma, laryngeal edema and angioneurotic edema; with long-term use — skin pigmentation, and lenticular and corneal opacities. Injections of fluphenazine decanoate are extremely well tolerated, local tissue reactions occurring only rarely.

Overdosage:
It should be treated symptomatically and supportively. Extrapyramidal reactions will respond to oral or parenteral antiparkinsonian drug such as procyclidine or benztropine. In cases of severe hypotension, all procedures for the management of circulatory shock should be instituted, e.g. vasoconstrictors and/or intravenous fluids. However, only the vasoconstrictors metaraminol of noradrenaline should be used, as adrenaline may further lower the blood pressure through interaction with the phenothiazine.

Dispensing restrictions:
According to Hospital Physician's prescription or directions.

Storage:
Store below 25^0C and protect from light.
Do not keep in a refrigerator, since this will cause precipitation. If precipitation does occur, warming of the product before use to 37°C will dissolve the precipitate.
Detailed information about this drug has been circulated to the medical profession and is based on the reference book Physician' Desk Reference.

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Revised in August 2012 according to MOHs guidelines.