

Data Sheet

Name Of Medicine

Modecate

Modecate Concentrate

Fluphenazine decanoate

Presentation

Injection: Straw-coloured viscous liquid containing fluphenazine decanoate 12.5mg/0.5mL and 25mg/mL; 100mg/mL (Concentrate); in a sesame oil vehicle, with benzyl alcohol as preservative.

Uses

Actions

Fluphenazine decanoate is an esterified trifluoromethyl phenothiazine derivative. Chemically, fluphenazine is 4-(3-[2-(Trifluoromethyl) phenothiazin-10-yl]propyl)-1 piperazine. It is a highly potent antipsychotic agent with a markedly extended duration of action, available for intramuscular administration.

The basic effects of fluphenazine decanoate appear to be no different from those of fluphenazine hydrochloride. The only exception to this is a prolonged duration of action. The esterification of fluphenazine with decanoic acid markedly prolongs the drug's duration of effect without reducing its activity.

Like all phenothiazine derivatives, fluphenazine decanoate appears to act on the hypothalamus, depressing various components of the mesodiencephalic activating system which is involved in the control of basal metabolism and body temperature, wakefulness, vasomotor tone, emesis, and hormonal balance. In addition, the phenothiazines exert a peripheral autonomic affect to varying degrees. However, the site and mode of action of the phenothiazines have not been completely elucidated.

Fluphenazine and its ester derivatives differ from other phenothiazines in several respects; fluphenazine and its esters are more potent on a milligram basis, appear to be less sedating, and have less potentiating effect on central nervous system depressants and anaesthetics than do some of the other phenothiazine derivatives; they are less likely than some of the older phenothiazines to produce hypotension nevertheless, appropriate cautions should be observed. (See Precautions under Warnings and Precautions, and Adverse Effects).

A long-acting parenteral antipsychotic agent is an invaluable aid both to psychotic patients and to those who are responsible for them. Fluphenazine decanoate reduces hallucinations, delusions, confusion, withdrawal and, to a lesser degree, hostility and agitation. In general, the psychotic patient becomes more co-operative, less withdrawn, more responsive to social situations, and more receptive to psychotherapy or other non-chemotherapeutic measures. In the hospital, the nursing staff is relieved of the need for daily or even more frequent administration of drugs to a class of patients who may be difficult to treat and who frequently dispose of oral medication without swallowing it. In out-patient care, where constant supervision is rarely feasible, the longer interval between injections reduces the problem providing adequate maintenance dosage for patients who often fail to continue daily oral medication and consequently suffer frequent severe recurrences of acute psychotic episodes. Because maintenance medication can be more easily assured through the use of fluphenazine decanoate, it may be possible to release an increasing number of patients from custodial hospital care to an out-patient status.

Fluphenazine decanoate produces far fewer extrapyramidal side effects and a larger proportion of milder extrapyramidal side effects than any other fluphenazine product. A study conducted to determine the effects of fluphenazine decanoate revealed that out of 501 patients, 314 (62.7%) did not exhibit any extrapyramidal side effects. Out of the 187 patients who did show a variety of extrapyramidal side effects, 94 (50%) exhibited symptoms of only mild severity.

Pharmacokinetics

Interpatient variations in pharmacokinetics and in dose-response relationships may be influenced by age and genetics as well as by interaction with other agents.

Fluphenazine is extensively metabolized, undergoing "first pass" metabolism by the liver, and is excreted in both the urine and faeces. The degree of antipsychotic activity of the metabolites is still unknown. Fluphenazine is highly protein-bound (greater than 90%) in plasma. Esterification of fluphenazine with a long-chain fatty acid and dissolving it in a sesame seed oil vehicle delays diffusion and availability of free drug released from the oily depot site. Peak plasma concentration occurs within the first 24-hours after intramuscular injection of fluphenazine decanoate.

The onset of action generally appears between 24 to 72 hours after injection, and the effects of the drug on psychotic symptoms become significant within 48 to 96 hours. The therapeutic activity then continues for 1 to 4 weeks or longer with average duration of effect of between 3 to 4 weeks. The serum half-life is approximately 7-10 days.

Indications

Fluphenazine decanoate is indicated in the long-term management of psychotic disorders including schizophrenia, mania and organic brain syndrome. It is of particular value in the treatment of chronic schizophrenia and for patients who are unreliable at taking oral medication. The drug often alleviates such target symptoms as hallucinations, delusions, confusion and withdrawal. It is not only useful in the hospital milieu but is unparalleled, because of its long duration of action in the long-term maintenance therapy of chronically psychotic patients who are amenable to out-patient therapy.

Fluphenazine decanoate has not been shown to be effective in the management of behavioural complications in patients with mental retardation.

Dosage And Administration

Note: Modecate Concentrate (100mg in 1mL) is not to be confused with the less potent dosage presentations of Modecate 12.5mg in 0.5mL and 25mg in 1mL. Modecate should be administered under the supervision of only those who are experienced in the clinical use of neuroleptic agents. The optimal amount of fluphenazine decanoate 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. The response to Modecate and Modecate Concentrate may be delayed (see below) and if the medication is withdrawn it may take several weeks for symptoms to become apparent.

Fluphenazine decanoate injections are given intramuscularly. A dry syringe and needle of at least 21 gauge should be used. Use of a wet needle or syringe may cause solution to become cloudy.

To begin therapy with Modecate the following regimens are suggested:

For most patients, a dose of 12.5 to 25mg 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 a 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 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 stabilised on a fixed daily dosage of fluphenazine hydrochloride tablets or fluphenazine hydrochloride elixir, conversion of therapy from these short-acting oral forms to the long-acting injectable fluphenazine decanoate may be indicated.

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

Once conversion to fluphenazine decanoate 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 with a rapid-acting phenothiazine compound . When acute symptoms have subsided, 25mg of Modecate may be administered; subsequent dosage is adjusted as necessary.

'Poor risk' patients (those with known hypersensitivity to phenothiazines, or with disorders that predispose to undue reactions): Therapy may be initiated cautiously with oral fluphenazine hydrochloride. When the pharmacological effects and an appropriate dosage are apparent, an equivalent dose of fluphenazine decanoate may be administered. Subsequent dosage adjustments are made in accordance with the response of the patient.

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 100mg. If doses greater than 50mg are deemed necessary, the next dose and succeeding doses should be increased cautiously in increments of 12.5mg.

Use in the elderly

Antipsychotic medication should be used with care in elderly patients (>60 years old), as these patients have a greater potential for adverse effects.

Doses in the lower range (1/4 to 1/3 of those in younger adults) should be sufficient for most elderly patients. Response should be monitored and dose adjusted. If an increase is

necessary, doses should be gradually increased.

Contraindications

Modecate is contraindicated in patients with marked cerebral atherosclerosis, suspected or established subcortical brain damage, blood dyscrasias, phaeochromocytoma, severe cardiac insufficiency or renal or liver damage. Modecate is further contraindicated in comatosed patients, those in severely depressed states or patients receiving large doses of CNS depressants (alcohol, barbiturates, narcotics, hypnotics etc). It is not recommended for the treatment of anxiety and tension states or geriatric confusion and agitation.

Modecate is contraindicated in patients who have shown hypersensitivity to the active and inactive ingredients. Caution should be observed in patients with a history of sensitivity to other phenothiazines, as cross-sensitivity may occur.

Fluphenazine decanoate is not intended for use in children under 12 years of age.

Warnings And Precautions

The use of Modecate may impair the mental and physical abilities required for driving a car or operating heavy machinery. Potentiation of the effects of alcohol may occur with the use of this medication.

Abrupt Withdrawal

In general, phenothiazines do not produce psychic dependence; however, gastritis, nausea and vomiting, dizziness, and tremulousness have been reported following abrupt cessation of dose therapy. Reports suggest that these symptoms can be reduced if concomitant antiparkinson agents are continued for several weeks after the phenothiazine is withdrawn.

Prolongation of the QT interval

Since phenothiazines can prolong the QT interval, caution should be used when treating patients with cardiovascular disease, or congenital or acquired QT interval prolongation. Concomitant treatment with other drugs known to cause QT prolongation should be avoided. (See **Warnings and Precautions – Drug Interactions and Adverse Effects – Other Reactions.**)

Cerebrovascular Events

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. Fluphenazine should be used with caution in patients with risk factors for stroke.

Venous thromboembolism:

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all

possible risk factors for VTE should be identified before and during treatment with fluphenazine decanoate and preventive measures undertaken.

Increased Mortality in Elderly People with Dementia:

Data from two large observational studies showed that elderly people with dementia who are treated with antipsychotics are at a small increased risk of death compared with those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known.

Tardive dyskinesia (TD)

A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with neuroleptic (antipsychotic) drugs, including fluphenazine. 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.

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, including fluphenazine, 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 occurrence of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is 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 sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear 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

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic agents. 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 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.

Use in Pregnancy

The safe use of Modecate during pregnancy has not been established. Modecate should be used during pregnancy only if the anticipated benefit outweighs the risk and the administered dose and duration of treatment should be as low and as short as possible.

Neonates exposed to antipsychotic drugs (including fluphenazine) during the third trimester of pregnancy are at risk of experiencing extrapyramidal neurological disturbances and/or withdrawal symptoms following delivery. There have been post-market 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 additional medical treatment or monitoring.

Other

Elderly Patients with Dementia-related Psychosis

In elderly patients with dementia-related psychosis, the efficacy of fluphenazine decanoate has not been established. Observational studies suggest that elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Risk factors that may predispose this patient population to increased risk of death when treated with antipsychotics include age >80 years, sedation, concomitant use of benzodiazepines, or presence of pulmonary conditions (e.g. pneumonia, with or without aspiration)

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.

Liver or kidney damage, rarely manifested by cholestatic jaundice, may be encountered during therapy. Treatment should be discontinued if this occurs. Alteration in cephalin flocculation or alkaline phosphatase and/or increased thymol turbidity (without or with leucocytosis), sometimes accompanied by abnormalities in other liver function tests, have been reported in patients receiving fluphenazine decanoate who have had no clinical evidence of liver damage. This, however is not uncommon with phenothiazine therapy.

Renal function of patients on long-term therapy should be monitored; if BUN (blood urea nitrogen) becomes abnormal, treatment should be discontinued.

Routine blood counts are advisable on long-term therapy since rare instances of blood dyscrasias including leucopenia, agranulocytosis, thrombocytopenic or

non-thrombocytopenia purpura, eosinophilia, and pancytopenia have been reported with phenothiazine derivatives. If any soreness of the mouth, gums or throat, or any symptoms of upper respiratory infection occur and a leucocyte count confirms cellular depression; therapy should be discontinued and appropriate measures instituted immediately.

Modecate should be used with caution in patients exposed to extreme heat or phosphorus insecticides; in patients with epilepsy, a history of convulsive disorders or conditions predisposing to epilepsy, (since grand mal seizures have been known to occur); in patients with special medical disorders such as mitral insufficiency, cardiac arrhythmias or other cardiovascular diseases; in patients with severe respiratory disease or thyrotoxicosis and in patients who have exhibited idiosyncrasy to other centrally-acting drugs.

When undergoing surgery, psychotic patients on large doses of phenothiazine preparation should be watched carefully for possible hypotensive phenomena. Moreover, it should be remembered that a reduction in dosage of anaesthetic or central nervous system depressants may be required.

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

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

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 the patient's hepatic function, renal function and haematological status.

Caution should be exercised in those who have marked extrapyramidal reactions to oral phenothiazines or similar drugs, particularly elderly females. Such patients should start on half the normal dose.

Neuroleptic medication elevates 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.

Benzyl alcohol and sesame oil (Excipients):

This product contains 15 mg of benzyl alcohol per mL. Benzyl alcohol must not be given to premature babies or neonates. It may cause toxic reactions and anaphylactoid reactions in infants and children up to three years old. This product contains sesame oil, which may rarely cause severe allergic reactions.

Drug Interactions

The possibility should be borne in mind that phenothiazines may:

Increase the central nervous system depression produced by drugs such as alcohol, hypnotics, sedatives or strong analgesics.

Antagonize the action of adrenaline and other sympathomimetic agents and reverse the blood-pressure-lowering effects of adrenergic-blocking agents such as guanethidine and clonidine.

Impair:

- a) the anti-Parkinsonian effect of L-Dopa;
- b) the effect of anti-convulsants;
- c) the metabolism of tricyclic antidepressants;
- d) the control of diabetes.

Increase the effect of anticoagulants.

Interact with lithium and its salts in terms predisposing to adverse reactions.

Interact with anticholinergic drugs with possible enhancement of its anticholinergic effects. For example, an anti-Parkinson drug, such as benserazide, used to manage extrapyramidal side effects, may exacerbate the antimuscarinic effects of fluphenazine.

Enhance the cardiac depressant effects of quinidine.

Enhance the absorption of corticosteroids, digoxin and neuromuscular blocking agents.

Give false results on pregnancy tests.

Other specific drug interactions are as follows:

Amphetamine/Anorectic Agents: Concurrent administration may produce antagonistic pharmacologic effects.

Cimetidine: Cimetidine may reduce plasma concentrations of phenothiazines.

Antacids/Antidiarrheal agents: Concurrent administration may interfere with fluphenazine absorption. Administration of antacids should be spaced at least 1 hour before or 2-3 hours after fluphenazine dose.

Medicines that prolong the QT Interval: Medicines that can prolong the QT interval should be avoided, as should any medicine that can cause electrolyte imbalance or an increase in the concentration of fluphenazine in the blood.

P450 Enzyme substrates or inhibitors: Fluphenazine is metabolized by P450 2D6 and is itself an inhibitor of this drug-metabolizing enzyme. The plasma concentrations and the effects of fluphenazine may therefore be increased and prolonged by drugs that are either the substrates or inhibitors of this P450 isoform, possibly resulting in cardiac toxicity, anticholinergic side effects, or orthostatic hypotension.

ACE inhibitors/Thiazide Diuretics: Hypotension may result via additive or synergistic pharmacological activity.

Beta Blockers: Plasma levels of both drugs may be increased. Dosage reduction of both drugs is recommended.

Anticonvulsants: Anticonvulsant action may be impaired by Modecate.

Adverse Effects

Central Nervous System

The side effects more frequently reported with phenothiazine compounds and other antipsychotic agents are extrapyramidal symptoms such as pseudo-parkinsonism (tremor, rigidity, etc), akathisia, dystonia, dyskinesia, oculogyric crisis, and opisthotonos etc. They are *usually reversible*; however, a persistent pseudo-parkinsonian syndrome may develop after prolonged administration of phenothiazines. Extrapyramidal reactions may be alarming, and the patient should be forewarned and reassured. These reactions can usually be controlled by administration of anti-parkinsonism drugs (such as benzotropine mesylate) and if necessary, reduction in dosage.

Tardive Dyskinesia

This syndrome is characterised by rhythmic, stereo-typed, dyskinetic, involuntary movements (particularly of the face, mouth, tongue and jaw) which resemble the facial grimaces of encephalitis. These may be accompanied by choreiform movements of the limbs. In these chronic cases, the symptoms may persist after drug withdrawal and appear to be irreversible in some patients. Anti-parkinsonian agents may not be of benefit in these instances. The risk of developing this persistent syndrome appears to be greatest in elderly female patients with organic brain disease or damage, who have been receiving fairly large doses of phenothiazines for a prolonged period. 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 manoeuvre 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. Leukocytosis, elevated CPK, liver function abnormalities, and acute renal failure may also occur with NMS.

A reduction in dosage or symptomatic treatment may be necessary to relieve drowsiness, lethargy, or depression, if they occur. Impairment of judgement and mental skills and

epileptiform attacks are occasionally seen. As with other phenothiazines, reactivation or aggravation of psychotic processes may be encountered. Phenothiazine derivatives have been known to cause restlessness, excitement, or bizarre dreams in some patients. Alterations in electroencephalographic tracings or cerebrospinal fluid proteins may occur; cerebral oedema may rarely occur.

Autonomic Nervous System

Hypotension has rarely presented a problem with fluphenazines. However, patients with phaeochromocytoma, cerebral vascular or renal insufficiency, or a severe cardiac reserve deficiency such as may occur in mitral insufficiency, appear to be particularly prone to hypotensive reactions with phenothiazines; they 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. Noradrenaline tartrate is the most suitable agent for this purpose; adrenaline should not be used since phenothiazine derivatives have been found to reverse its action, further lowering of blood pressure (that is, neuroleptics block peripheral alpha adrenergic receptors thus inhibiting the alpha vasoconstricting effects of adrenaline and leaving the beta-vasodilator effect relatively unopposed).

Hypertension and fluctuations in blood pressure have been reported with phenothiazines.

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, faecal impaction, paralytic ileus, tachycardia or nasal congestion.

Metabolic and Endocrine System

Weight change, peripheral oedema, abnormal lactation, gynaecomastia, 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, seborrhoea, photosensitivity, eczema and even exfoliative dermatitis have been reported with phenothiazine derivatives. The possibility of anaphylactic reactions occurring in some patients should be borne in mind. Asthma, laryngeal edema, and angioneurotic edema may rarely occur.

Haematologic

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 bone marrow

depression, therapy should be discontinued and other appropriate measures instituted immediately.

Hepatic

Cholestatic jaundice has been encountered with fluphenazine treatment, particularly during the first months of therapy. Treatment should be discontinued if jaundice occurs. Alterations in liver function tests have been reported in patients receiving fluphenazine who have had no clinical evidence of liver damage.

Other Reactions

Sudden, unexpected and unexplained deaths have been reported in hospitalised 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 behaviour patterns shortly before death. Autopsy findings in these cases have usually revealed acute fulminating pneumonia or pneumonitis, aspiration of gastric contents, or intramyocardial lesions. Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis, have been reported with antipsychotic drugs.

Although this is not a general feature of fluphenazine, potentiation of central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol) may occur - See Precautions under **Warnings and Precautions** for patients undergoing surgery.

The following adverse reactions have also occurred with phenothiazine derivatives; hypotension severe enough to cause fatal cardiac arrest, ECG changes particularly prolongation of the QT interval which may lead to serious arrhythmias, disturbances of body temperature (hypo- and hyperthermic), potentiation of reactions to extreme heat, potentiation of reactions to phosphorus insecticides, asthma, laryngeal oedema, angioneurotic oedema, pigmentary retinopathy, systemic lupus erythematosus-like syndrome; with long-term use, skin pigmentation, and lenticular and corneal opacities have also occurred. Injections of fluphenazine decanoate are extremely well tolerated locally and tissue reactions occur only rarely.

Pharmaceutical Precautions

Do not store above 25 degrees C. Do not refrigerate or freeze. Protect from direct sunlight. With exposure to low temperatures a precipitate may form which will re-dissolve on warming to room temperature.

As another phenothiazine, chlorpromazine may cause severe dermatitis in sensitised persons it is recommended that pharmacists, nurses and others who handle Modecate frequently should avoid skin contact with fluphenazine.

Medicine Classification

Prescription Medicine

Package Quantities

Injection, 12.5mg/0.5mL, 25mg/1mL, and 100mg/1mL, 5s.

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