Thioridazine hydrochloride tablets should be avoided in children and other patients who are known to be sensitive to thioridazine hydrochloride tablets.

ADVERSE REACTIONS: The most frequently observed adverse reactions are sedation, drowsiness, hypotension, hypotonic weakness, extrapyramidal reactions, drooling, urinary retention, and convulsions. These side effects are generally dose-related and may be prevented by reducing the dosage. Other adverse reactions include: gastrointestinal—nausea, vomiting, anorexia, constipation, dry mouth, mild abdominal pain; cardiovascular—postural hypotension, tachycardia; respiratory—dyspnea, apnea, bronchospasm; urinary—proteinuria, hematuria, urinary retention, bladder atony; central nervous system—headache, dizziness, paresthesia, somnolence, lethargy, ataxia, tremor, disorientation, agitation, confusion, hallucinations, delirium, convulsions, coma, depression, manic episodes, and extrapyramidal symptoms; other—fever, vasomotor rhinitis, sinusitis, dental problems, contact dermatitis, dermatitis herpetiformis, xerostomia, anaphylaxis, angioedema, Raynaud’s phenomenon, hirsutism, and hypertrichosis.

DESCRIPTION: Thioridazine hydrochloride is a 2-methylmercapto-1-(2-(N-methyl-N-propyl)ethyl)piperazine-1-carboxylic acid derivative. Each 25 mg tablet contains 25 mg of thioridazine hydrochloride USP, 5 mg of phenylephrine hydrochloride USP, and 0.1 mg of methylparaben USP. Each 50 mg tablet contains 50 mg of thioridazine hydrochloride USP, 10 mg of phenylephrine hydrochloride USP, and 0.2 mg of methylparaben USP. Each 100 mg tablet contains 100 mg of thioridazine hydrochloride USP, 20 mg of phenylephrine hydrochloride USP, and 0.4 mg of methylparaben USP. Thioridazine hydrochloride tablets, USP, 10 mg, 25 mg, 50 mg, and 100 mg are available in unit dose blister packages of 100 (10 cards of 10 tablets each). Thioridazine hydrochloride oral solution, USP, 50 mg per 5mL, is available in 15mL, 30mL, and 60mL bottles and a 60mL unflavored parenteral formulation, USP. Thioridazine hydrochloride oral solution, USP, 10 mg per 5mL, is also available in 45mL bottles.

STORAGE: Store at 25° to 30°C (77° to 86°F) [See USP Controlled Room Temperature]. Protect from light.

**Trademarks of Medical Economics Company, Inc.**

**Manufactured by:**

Mylan Pharmaceuticals Inc., Morgantown, WV 26505 U.S.A.

**Distributed by:**

Mylan Inc., Rostraver, PA 15074 U.S.A.

S-4853 1/13

**WARNING:** Thioridazine has been shown to prolong the QT interval in a dose-dependent fashion. This effect may be increased by concomitant use of other drugs that also prolong the QT interval, such as thioridazine plus antipsychotic drugs. Due to this risk, thioridazine should be avoided in patients with congenital long QT syndrome or a history of cardiac arrhythmias. Thioridazine use should be avoided in patients with a known risk for QT prolongation (e.g., electrolyte disturbances and certain drug interactions). Reduced cytochrome P450 2D6 isozyme activity drugs that inhibit this isozyme (e.g., clomipramine, cimetidine, and disopyramide) may increase the risk of QT prolongation associated with thioridazine. Due to the additive effect of coadministration with other drugs known to prolong the QT interval, thioridazine should be used with caution in patients with congenital long QT syndrome or a history of cardiac arrhythmias. Such an increased risk may result also from the additive effect of concomitantly using other agents that prolong the QT interval. Thioridazine is contraindicated with these drugs as well as patients, comprising about 7% of the normal population, who are known to have a preexisting long QT interval. Noncardiovascular depolarizing agents may also be used to induce ventricular fibrillation. Therefore, the use of agents that prolong the QT interval should be avoided. In common with other phenothiazines, thioridazine is contraindicated in severe chronic respiratory depression or narcotic respiratory depression together with one or more of the following therapeutic interventions: correction of electrolyte abnormalities and acute acid-base imbalances, ischemia, hypoxia, and cerebral hypoperfusion and/or hypovolemia, and ventilator pacing and disobliteration. Disobstructive, procainamide, and quinidine may potentiate QT interval changes when administered with other agents that prolong the QT interval (see WARNINGS and PRECAUTIONS). Caution is strongly recommended when administering bilobec, as it may increase the risk of developing ventricular tachycardia. Treatment of hypokalemia may result in intravascular fluid and venous pooling. Phenothiazines, levodopa, or metaraminol are the appropriate pressor agents for use in the management of hypotensive hypothermia. The use of antihypertensive blocking agents of the phenothiazines has been associated with the development of orthostatic hypotension and other sequelae of hypotension in elderly patients with cardiovascular disease or diabetes. Postural variation may range. In addition, it is reasonable to expect that the additional impairment of orthostatic hypotension might be additive to those of thioridazine, resulting in problematic hypotension.

In managing overdose, venous bleeding and anticoagulant therapy are generally avoided in patients with multiple drug involvement. Calcium gluconate and repeated doses of activated charcoal should be given. In the presence of hypotension, potential vasodilation may result. Treatment should not be instituted in patients expected to develop refractory, or those who require more than 20% dilution in the clinical treatment of refractory schizophrenia, their efficacy in such patients is unknown. INDICATIONS AND USAGE: The usual starting dose for adult schizophrenic patients is 50 mg to 100 mg thioridazine hydrochloride tablets. Dosage should be individualized and the smallest effective dosage should be determined for each patient. The usual starting dose for adult schizophrenic patients is 10 mg to 25 mg thioridazine hydrochloride tablets, with a gradual increase to a maximum of 100 mg daily in divided doses. The dosage of thioridazine hydrochloride tablets should be reduced gradually to determine the minimum maintenance dose. The total daily dosage range is 200 to 600 mg, divided into four doses. Pediatric Patients: For pediatric patients with schizophrenia who are responsive to other agents, the recommended initial dose is 5 mg/kg/day given in divided doses. Dosage may need to be increased gradually until therapeutic effective is obtained or the maximum dose of 3 mg/kg/day has been reached.

DOSE AND ADMINISTRATION: Since thioridazine hydrochloride tablets are associated with a risk of prolongation of the QT interval, which at a potential life-threatening risk, it is strongly recommended that a patient be given at least two tria ls, each with a different antipsychotic drug. Dose should be reduced gradually to determine the minimum maintenance dose. The total daily dosage range is 200 to 600 mg, divided into four doses.

Adoles: The usual starting dose for adult schizophrenic patients is 10 mg to 25 mg thioridazine hydrochloride tablets, with a gradual increase to a maximum of 100 mg daily in divided doses. The dosage of thioridazine hydrochloride tablets should be reduced gradually to determine the minimum maintenance dose. The total daily dosage range is 200 to 600 mg, divided into four doses. Pediatric Patients: For pediatric patients with schizophrenia who are responsive to other agents, the recommended initial dose is 10 mg/m²/day given in divided doses. Dosage may need to be increased gradually until therapeutic effective is obtained or the maximum dose of 3 mg/kg/day has been reached.

DOSAGE AND ADMINISTRATION: Since thioridazine hydrochloride tablets are associated with a risk of prolongation of the QT interval, which at a potential life-threatening risk, it is strongly recommended that a patient be given at least two trials, each with a different antipsychotic drug. Dose should be reduced gradually to determine the minimum maintenance dose. The total daily dosage range is 200 to 600 mg, divided into four doses.

ADVERSE REACTIONS: The most frequently observed adverse reactions are sedation, drowsiness, hypotension, hypotonic weakness, extrapyramidal reactions, drooling, urinary retention, and convulsions. These side effects are generally dose-related and may be prevented by reducing the dosage. Other adverse reactions include: gastrointestinal—nausea, vomiting, anorexia, constipation, dry mouth, mild abdominal pain; cardiovascular—postural hypotension, tachycardia; respiratory—dyspnea, apnea, bronchospasm; urinary—proteinuria, hematuria, urinary retention, bladder atony; central nervous system—headache, dizziness, paresthesia, somnolence, lethargy, ataxia, tremor, disorientation, agitation, confusion, hallucinations, delirium, convulsions, coma, depression, manic episodes, and extrapyramidal symptoms; other—fever, vasomotor rhinitis, sinusitis, dental problems, contact dermatitis, dermatitis herpetiformis, xerostomia, anaphylaxis, angioedema, Raynaud’s phenomenon, hirsutism, and hypertrichosis.

DESCRIPTION: Thioridazine hydrochloride is a 2-methylmercapto-1-(2-(N-methyl-N-propyl)ethyl)piperazine-1-carboxylic acid derivative. Each 25 mg tablet contains 25 mg of thioridazine hydrochloride USP, 5 mg of phenylephrine hydrochloride USP, and 0.1 mg of methylparaben USP. Each 50 mg tablet contains 50 mg of thioridazine hydrochloride USP, 10 mg of phenylephrine hydrochloride USP, and 0.2 mg of methylparaben USP. Each 100 mg tablet contains 100 mg of thioridazine hydrochloride USP, 20 mg of phenylephrine hydrochloride USP, and 0.4 mg of methylparaben USP. Thioridazine hydrochloride tablets, USP, 10 mg, 25 mg, 50 mg, and 100 mg are available in unit dose blister packages of 100 (10 cards of 10 tablets each). Thioridazine hydrochloride oral solution, USP, 50 mg per 5mL, is available in 15mL, 30mL, and 60mL bottles and a 60mL unflavored parenteral formulation, USP. Thioridazine hydrochloride oral solution, USP, 10 mg per 5mL, is also available in 45mL bottles.

STORAGE: Store at 25° to 30°C (77° to 86°F) [See USP Controlled Room Temperature]. Protect from light.
REACTIONS.

Drug-induced hypotension in patients treated with thioridazine has been reported. In patients where large doses are given early in treatment. Generally, this effect tends to diminish as treatment with thioridazine continues. Hence, a dosage adjustment may be required. Some patients may require antihypertensive therapy. Aortic and mitral valvular regurgitations may develop in patients treated with thioridazine. Pigmentation of areas of the skin or conjunctiva may develop. A peculiar skin-eye syndrome has been reported. The syndrome (tongue, puffing of cheeks, puckering of the mouth, chewing movements), trunk, and extremities. The severity of the syndrome and the degree of impairment produced vary in different patients. Observation for several days may be required.

Drug-induced hypotension may be marked by progressive pigmentation of areas of the skin or conjunctiva. The syndrome may include a peculiar skin-eye syndrome with marked involvement of the face, tongue, and conjunctiva. Given these considerations, antipsychotics should be prescribed in a manner that allows the patient to titrate his own dose as tolerated.

It has been suggested in regard to phenothiazines that central anticholinergic symptoms may occur in a patient treated with phenothiazines. Sometimes these symptoms may occur in a patient treated with phenothiazines. However, in view of the dosedependency of these symptoms, it may be argued that the symptoms are dose-related. The symptoms may be minimized by reduction of the dose. Careful consideration of dose and the duration of treatment producing a satisfactory clinical response should be made.

The syndrome may occur in patients treated with thioridazine. In patients where large doses are given early in treatment. Generally, this effect tends to diminish as treatment with thioridazine continues. Hence, a dosage adjustment may be required. Some patients may require antihypertensive therapy. Aortic and mitral valvular regurgitations may develop in patients treated with thioridazine. Pigmentation of areas of the skin or conjunctiva may develop. A peculiar skin-eye syndrome has been reported. The syndrome (tongue, puffing of cheeks, puckering of the mouth, chewing movements), trunk, and extremities. The severity of the syndrome and the degree of impairment produced vary in different patients. Observation for several days may be required.

Drug-induced hypotension may be marked by progressive pigmentation of areas of the skin or conjunctiva. The syndrome may include a peculiar skin-eye syndrome with marked involvement of the face, tongue, and conjunctiva. Given these considerations, antipsychotics should be prescribed in a manner that allows the patient to titrate his own dose as tolerated.

It has been suggested in regard to phenothiazines that central anticholinergic symptoms may occur in a patient treated with phenothiazines. Sometimes these symptoms may occur in a patient treated with phenothiazines. However, in view of the dosedependency of these symptoms, it may be argued that the symptoms are dose-related. The symptoms may be minimized by reduction of the dose. Careful consideration of dose and the duration of treatment producing a satisfactory clinical response should be made.

The syndrome may occur in patients treated with thioridazine. In patients where large doses are given early in treatment. Generally, this effect tends to diminish as treatment with thioridazine continues. Hence, a dosage adjustment may be required. Some patients may require antihypertensive therapy. Aortic and mitral valvular regurgitations may develop in patients treated with thioridazine. Pigmentation of areas of the skin or conjunctiva may develop. A peculiar skin-eye syndrome has been reported. The syndrome (tongue, puffing of cheeks, puckering of the mouth, chewing movements), trunk, and extremities. The severity of the syndrome and the degree of impairment produced vary in different patients. Observation for several days may be required.

Drug-induced hypotension may be marked by progressive pigmentation of areas of the skin or conjunctiva. The syndrome may include a peculiar skin-eye syndrome with marked involvement of the face, tongue, and conjunctiva. Given these considerations, antipsychotics should be prescribed in a manner that allows the patient to titrate his own dose as tolerated.

It has been suggested in regard to phenothiazines that central anticholinergic symptoms may occur in a patient treated with phenothiazines. Sometimes these symptoms may occur in a patient treated with phenothiazines. However, in view of the dosedependency of these symptoms, it may be argued that the symptoms are dose-related. The symptoms may be minimized by reduction of the dose. Careful consideration of dose and the duration of treatment producing a satisfactory clinical response should be made.

The syndrome may occur in patients treated with thioridazine. In patients where large doses are given early in treatment. Generally, this effect tends to diminish as treatment with thioridazine continues. Hence, a dosage adjustment may be required. Some patients may require antihypertensive therapy. Aortic and mitral valvular regurgitations may develop in patients treated with thioridazine. Pigmentation of areas of the skin or conjunctiva may develop. A peculiar skin-eye syndrome has been reported. The syndrome (tongue, puffing of cheeks, puckering of the mouth, chewing movements), trunk, and extremities. The severity of the syndrome and the degree of impairment produced vary in different patients. Observation for several days may be required.

Drug-induced hypotension may be marked by progressive pigmentation of areas of the skin or conjunctiva. The syndrome may include a peculiar skin-eye syndrome with marked involvement of the face, tongue, and conjunctiva. Given these considerations, antipsychotics should be prescribed in a manner that allows the patient to titrate his own dose as tolerated.

It has been suggested in regard to phenothiazines that central anticholinergic symptoms may occur in a patient treated with phenothiazines. Sometimes these symptoms may occur in a patient treated with phenothiazines. However, in view of the dosedependency of these symptoms, it may be argued that the symptoms are dose-related. The symptoms may be minimized by reduction of the dose. Careful consideration of dose and the duration of treatment producing a satisfactory clinical response should be made.

The syndrome may occur in patients treated with thioridazine. In patients where large doses are given early in treatment. Generally, this effect tends to diminish as treatment with thioridazine continues. Hence, a dosage adjustment may be required. Some patients may require antihypertensive therapy. Aortic and mitral valvular regurgitations may develop in patients treated with thioridazine. Pigmentation of areas of the skin or conjunctiva may develop. A peculiar skin-eye syndrome has been reported. The syndrome (tongue, puffing of cheeks, puckering of the mouth, chewing movements), trunk, and extremities. The severity of the syndrome and the degree of impairment produced vary in different patients. Observation for several days may be required.

Drug-induced hypotension may be marked by progressive pigmentation of areas of the skin or conjunctiva. The syndrome may include a peculiar skin-eye syndrome with marked involvement of the face, tongue, and conjunctiva. Given these considerations, antipsychotics should be prescribed in a manner that allows the patient to titrate his own dose as tolerated.

It has been suggested in regard to phenothiazines that central anticholinergic symptoms may occur in a patient treated with phenothiazines. Sometimes these symptoms may occur in a patient treated with phenothiazines. However, in view of the dosedependency of these symptoms, it may be argued that the symptoms are dose-related. The symptoms may be minimized by reduction of the dose. Careful consideration of dose and the duration of treatment producing a satisfactory clinical response should be made.

The syndrome may occur in patients treated with thioridazine. In patients where large doses are given early in treatment. Generally, this effect tends to diminish as treatment with thioridazine continues. Hence, a dosage adjustment may be required. Some patients may require antihypertensive therapy. Aortic and mitral valvular regurgitations may develop in patients treated with thioridazine. Pigmentation of areas of the skin or conjunctiva may develop. A peculiar skin-eye syndrome has been reported. The syndrome (tongue, puffing of cheeks, puckering of the mouth, chewing movements), trunk, and extremities. The severity of the syndrome and the degree of impairment produced vary in different patients. Observation for several days may be required.
Cardiovascular monitoring should commence immediately and should include con- tinuous electrocardiographic monitoring to detect possible arrhythmias. Treatment may include one or more of the following therapeutic interventions: correction of electrolyte abnormalities and acid-base balance, lidocaine, phenytoin, propranolol, or verapamil and pacing and defibrillation. Diaphoresis, procainamide, and quinidine may provide additional D1 antagonizing effects when administered in patterns with acute myocardial ischemia and sustained ventricular tachycardia (see CONTRAINDICATIONS). Caution must be observed when administering lidocaine, as it may increase the risk of developing toxicity.

Treatment of hypotension may require intravenous fluids and vasopressors. Phenytoin, lidocaine, or other agents are the appropriate pressor agents for use in the management of refractory hypotension. The patient is a uniform blocking

doses. Dosage may be increased gradually until optimum therapeutic effect is

Pediatric Patients:

reduced gradually to determine the minimum maintenance dose. The total daily

necessary. Once effective control of symptoms has been achieved, the dosage may be

10 mg, 25 mg, 50 mg or 100 mg of thioridazine hydrochloride, USP.

HOW SUPPLIED:

Adults:

three times a day, with a gradual increment to a maximum of 800 mg daily if nec-

patient (see INDICATIONS and WARNINGS).

Since thioridazine hydrochloride tablets are asso-

and ß adrenergic agonist properties inappropriate, including epinephrine and

should be considered. Induction of emesis is less preferable to gastric lavage

from a certified Regional Poison Control Center. Telephone numbers of certified

up-to-date information about the treatment of overdose can often be obtained

Increased Mortality in Elderly Patients with Dementia-Related Psychosis: Mard

patients and the administration of pimozide with antipsychotics may increase mor-

infectious (e.g., pneumonia) in nature. Observational studies suggest that,

contraining drugs may increase mortality. The extent to which the findings of

chotic drug as opposed to some characteristic(s) of the patients is not clear.

Thioridazine hydrochloride is not approved for the treatment of patients with

molecular formula are:

Thioridazine hydrochloride tablets are indicated for the

the following ingredients: Magnesium stearate, starch, talasseine cellulose, polyethylene glycol, sodium lauryl sulfate and titanium dioxide.

The basic pharmacological activity of thioridazine is

Prolongation of the QTc interval has been associated with the ability to cause Tor-

resulting elevated levels of thioridazine would be expected to augment the pro-

patients with congenital long QT syndrome or a history of cardiac arrhythmias.

In addition to the above, thioridazine tablets have not been systematically evaluated in controlled trials in treatment refractory schiz-

TRIALS IN THE TREATMENT OF REFRACTORY SCHIZOPHRENIC PATIENTS AND

The patient should be given

CONTRAINDICATIONS). However, the prescriber should be aware that thioridazine

NOTICE: The contraindications to thioridazine should be reserved for use in the treat-

indications for the use of this drug. Thioridazine hydrochloride tablets should be used only in patients who have failed to respond adequately to treatment with adequate doses of other antipsychotic drugs, other than those contraindications for the use of thioridazine hydrochloride tablets. It is strongly recommended that a patient be given at least one other antipsychotic drug product, at an adequate dose, and for an adequate duration (see WARNINGS and CONTRAINDICATIONS).

CONCOMITANT DRUGS: The concomitant use of thioridazine with other drugs known to be potentially antiarrhythmic or to prolong the QT interval, such as pimozide, is not recommended. Although the concomitant use of thioridazine hydrochloride tablets with other drugs should be avoided, clinical experience suggests that no interaction other than minor clinical effects has been observed.

Thioridazine is not approved for the treatment of patients with dementia-related psychosis (see WARNINGS). It should also be noted that hypertension or thyrotoxicosis has been occasionally observed in patients taking thioridazine hydrochloride tablets.