

Thioril

For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

Abbreviated Prescribing information for Thioril (Thioridazine tablet)

[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:

Mechanism of action: The basic pharmacological activity of thioridazine is similar to that of other phenothiazines, but is associated with minimal extrapyramidal stimulation. However, thioridazine has been shown to prolong the QTc interval in a dose dependent fashion. This effect may increase the risk of serious, potentially fatal, ventricular arrhythmias, such as Torsades de pointes type arrhythmias. Due to this risk, thioridazine is indicated only for schizophrenic patients who have not been responsive to or cannot tolerate other antipsychotic agents.

DOSAGE AND ADMINISTRATION: Since thioridazine hydrochloride tablets are associated with a dose related prolongation of the QTc interval, which is a potentially life threatening event, its use should be reserved for schizophrenic patients who fail to respond adequately to treatment with other antipsychotic drugs. Dosage must be individualized and the smallest effective dosage should be determined for each patient or as directed by the physician.

CONTRAINDICATION: Thioridazine is contra-indicated in patients with: Clinically significant cardiac disorders (e.g. cardiac failure, angina, cardiomyopathy or LV dysfunction): QTc interval prolongation, A history of ventricular arrhythmias or Torsades de Pointes, Bradycardia or 2nd or 3rd degree heart block, A family history of QTc interval prolongation, Uncorrected hypokalaemia or hypomagnesaemia. Prescribers should also note that thioridazine is metabolised by the cytochrome P450 2D6 pathway. Treatment is therefore contraindicated in patients known to have genetically determined reduced or no activity of cytochrome P450 2D6. Thioridazine is also contraindicated when patients are being prescribed other therapeutic agents known to be either substrates or the inhibitors of cytochrome P450 2D6. Because thioridazine prolongs the QTc interval in a concentration-related manner, it is also contraindicated with concurrent use of other drugs known to prolong the QTc interval. Thioridazine is also contra-indicated in patients with: Hypersensitivity to thioridazine HCl or other phenothiazines, thioridazine base or any of the other excipients, A history of hypersensitivity reactions, including severe photosensitivity, Comatose states, dementia and severe depression of the CNS, History of serious haematological conditions (e.g. bone marrow suppression).

WARNINGS & PRECAUTIONS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis, Potential for Proarrhythmic Effects, Tardive Dyskinesia Pregnancy Nonteratogenic Effects: Neonates exposed to antipsychotic drugs, during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery, (NMS), Central Nervous System Depressants

DRUG INTERACTION: Reduced cytochrome P450 2D6 isozyme activity, drugs which inhibit this isozyme (e.g., fluoxetine and paroxetine), and certain other drugs (e.g., fluvoxamine, propranolol, and pindolol) appear to appreciably inhibit the metabolism of thioridazine. The resulting elevated levels of thioridazine would be expected to augment the prolongation of the QTc interval associated with thioridazine and may increase the risk of serious, potentially fatal, cardiac arrhythmias, such as Torsades de pointes type arrhythmias. Such an increased risk may result also from the additive effect of coadministering thioridazine with other agents that prolong the QTc interval. Therefore, thioridazine is contraindicated with these drugs as well as in patients, comprising about 7% of the normal population, who are

known to have a genetic defect leading to reduced levels of activity of P450 2D6, Drugs That Inhibit Cytochrome P450 2D6, Drugs That Reduce the Clearance of Thioridazine Through Other Mechanisms Fluvoxamine: Propranolol, Pindolol, Drugs That Prolong the QTc Interval

ADVERSE REACTIONS: In the recommended dosage ranges with thioridazine hydrochloride most side effects are mild and transient. Drowsiness may be encountered on occasion, especially where large doses are given early in treatment. Generally, this effect tends to subside with continued therapy or a reduction in dosage. Pseudoparkinsonism and other extrapyramidal symptoms may occur but are infrequent. Nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache have been reported but are extremely rare, Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor have been seen, Endocrine System, Skin: Dermatitis and skin eruptions of the urticarial type have been observed infrequently. Photosensitivity is extremely rare, Cardiovascular System, Phenothiazine Derivatives, Autonomic Reactions, Cutaneous Reactions, Allergic Reactions, Hepatotoxicity, Cardiovascular Effects, Extrapyramidal Symptoms, Tardive Dyskinesia, Neuroleptic Malignant Syndrome (NMS), Endocrine Disturbances, Urinary Disturbances.

Manufactured by:

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TORRENT PHARMACEUTICALS LTD.

IN/THIORIL 10, 25, 50 mg/MAY-21/02/ABPI

(Additional information is available on request)