**PRESCRIBING INFORMATION**

# [Pr] Dom-METHIMAZOLE

Methimazole Tablets USP

5 mg

**Antithyroid Agent**

**DOMINION PHARMACAL**
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## NAME OF DRUG

**[Pr] Dom-METHIMAZOLE**

Methimazole Tablets USP

5 mg

## THERAPEUTIC CLASSIFICATION

Antithyroid Agent

## DESCRIPTION

Methimazole (1-methyl-2-mercaimidazole) is a white, crystalline substance that is freely soluble in water. It differs chemically from the drugs of the thiouracil series primarily because it has a five- instead of a six-membered ring.

Each tablet contains 5 mg methimazole, an orally administered antithyroid drug.

The molecular weight is 114.16, and the empirical formula is $C_4H_6N_2S$.

## ACTIONS

Methimazole inhibits the synthesis of thyroid hormones and thus is effective in the treatment of hyperthyroidism. The drug does not inactivate existing thyroxine and triiodo-thyronine that are stored in the thyroid or circulating in the blood, nor does it interfere with the effectiveness of thyroid hormones given by mouth or by injection.

The actions and use of methimazole are similar to those of propylthiouracil. On a weight basis, the drug is at least ten times as potent as propylthiouracil, but methimazole may be less consistent in action.
Methimazole is readily absorbed from the gastrointestinal tract. It is metabolized rapidly and requires frequent administration. Methimazole is excreted in the urine.

## INDICATIONS

Dom-METHIMAZOLE is indicated in the medical treatment of hyperthyroidism. Long-term therapy may lead to remission of the disease. Dom-METHIMAZOLE may be used to ameliorate hyperthyroidism in preparation for subtotal thyroidectomy or radioactive iodine therapy. Dom-METHIMAZOLE is also used when thyroidectomy is contraindicated or not advisable.

## CONTRAINDICATIONS

Methimazole is contraindicated in the presence of hypersensitivity to the drug and in nursing mothers because the drug is excreted in breast milk.

## WARNINGS

Agranulocytosis is potentially the most serious side effect of therapy with methimazole. Patients should be instructed to report to their physicians any symptoms of agranulocytosis, such as fever or sore throat. Leukopenia, thrombocytopenia, and aplastic anemia (pancytopenia) may also occur. The drug should be discontinued in the presence of agranulocytosis, aplastic anemia (pancytopenia), hepatitis, or exfoliative dermatitis. The patient's bone marrow function should be monitored.

Due to the similar hepatic toxicity profiles of methimazole and propylthiouracil, attention is drawn to the severe hepatic reactions which have occurred with both drugs. There have been rare reports of fulminant hepatitis, hepatic necrosis, encephalopathy, and death. Symptoms suggestive of hepatic dysfunction (anorexia, pruritis, right upper quadrant pain, etc) should prompt evaluation of liver function. Drug treatment should be discontinued promptly in the event of clinically significant evidence of liver abnormality including hepatic transaminase values exceeding 3 times the upper limit of normal.

Methimazole can cause fetal harm when administered to a pregnant woman. Methimazole readily croses the placental membranes and can induce goiter and even cretinism in the developing fetus. In addition, rare instances of aplasia cutis, as manifested by scalp defects have occurred in infants born to mothers who received methimazole during pregnancy. If methimazole is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be warned of the potential hazard to the fetus.

Since scalp defects have not been reported in offspring of patients treated with propylthiouracil, the agent may be preferable to methimazole in pregnant women requiring treatment with antithyroid drugs.

Postpartum patients receiving methimazole should not nurse their babies.

## PRECAUTIONS

*General*--Patients who receive methimazole should be under close surveillance and should be impressed wit the necessity of reporting immediately any evidence of illness, particularly sore throat, skin eruptions, fever, headache, or general malaise. In such cases, white-blood-cell and differential counts should be made to

determine whether agranulocytosis has developed. Particular care should be exercised with patients who are receiving additional drugs known to cause agranulocytosis.

*Laboratory Test*s--Because methimazole may cause hypoprothrombinemia and bleeding, prothrombin time should be monitored during therapy with the drug, especially before surgical procedures.
Periodic monitoring of thyroid function is warranted, and the finding of an elevated TSH warrants a decrease in the dosage of methimazole.

*Drug Interaction*s— The activity of anticoagulants may be potentiated by anti-vitamin-K activity attributed to methimazole.

*Carcinogenesis, Mutagenesis, Impairment of Fertility*--Rats treated for 2 years with methimazole demonstrated thyroid hyperplasia and thyroid adenoma and carcinoma formation. Such findings are seen with continuous suppression of thyroid function by sufficient doses of a variety of antithyroid agents. Pituitary adenomas have also been observed.

*Pregnancy*–Methimazole used judiciously is an effective drug in hyperthyroidism complicated by pregnancy. In many pregnant women, the thyroid dysfunction diminishes as the pregnancy proceeds; consequently, a reduction in dosage may be possible. In some instances, use of methimazole can be discontinued 2 or 3 weeks before delivery.

If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

*Nursing Mother*s--The drug appears in human breast milk and its use is contraindicated in nursing mothers.

*Usage in Childre*n--*See* Dosage and Administration.

## ADVERSE REACTIONS

Adverse reactions probably occur in less than 1 percent of patients.

Minor adverse reactions include skin rash, urticaria, nausea, vomiting, epigastric distress, arthralgia, paresthesia, loss of taste, abnormal loss of hair, myalgia, headache, pruritus, drowsiness, neuritis, edema, vertigo, skin pigmentation, jaundice, sialadenopathy, and lymphadenopathy.

Major adverse reactions (which occur with much less frequency than the minor adverse reactions) include inhibition of myelopoiesis (agranulocytosis, granulocytopenia, and thrombocytopenia), aplastic anemia, drug fever, a lupuslike syndrome, insulin autoimmune syndrome (which can result in hypoglycemic coma), hepatitis (jaundice may persist for several weeks after discontinuation of the drug), periarteritis, and hypoprothrombinemia. Nephritis occurs very rarely.

It should be noted that about 10% of patients with untreated hyperthyroidism have leukopenia (white-blood-cell count of less than 4,000/$mm^3$ ), often with relative granulopenia.

## OVERDOSAGE

Symptoms may include nausea, vomiting, epigastric distress, headache, fever, joint pain, pruritus, and edema. Aplastic anemia (pancytopenia) or agranulocytosis may be manifested in hours to days. Less frequent events are hepatitis, nephrotic syndrome, exfoliative dermatitis, neuropathies, and CNS stimulation or depression. Although not well studied, methimazole-induced agranulocytosis is generally associated with doses of 40 mg or more in patients older than 40 years of age.

No information is available on the median lethal dose of the drug or the concentration of methimazole in biologic fluids associated with toxicity and/or death.

*Treatmen*t--In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. The patient's bone marrow function should be monitored. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

Forced diuresis, peritoneal dialysis, hemodialysis, or charcoal hemoperfusion have not been established as beneficial for an overdose of methimazole.

## DOSAGE AND ADMINISTRATION

Dom-METHIMAZOLE is administered orally. It is usually given in three equal doses at approximately eight-hour intervals.

*Adul*t--The initial daily dosage is 15 mg for mild hyperthyroidism, 30 to 40 mg for moderately severe hyperthyroidism, and 60 mg for severe hyperthyroidism, divided into three doses at eight-hour intervals. The maintenance dosage is 5 to 15 mg daily.

*Pediatric*--Initially, the daily dosage is 0.4 mg/kg of body weight divided into three doses and given at eight-hour intervals. The maintenance dosage is approximately 1/2 of the initial dose.

## HOW SUPPLIED

Tablets, USP (scored): No. 1765, 5 mg, in bottles of 100. Identi-Code: J 94.