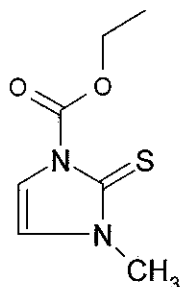


## **NEO-MERCAZOLE**

(carbimazole)

(CAS registry number: 22232-54-8)



The chemical name for carbimazole is ethyl 3 -methyl-2-thioxo-4-imidazoline-1-carboxylate. The chemical formula is  $C_7H_{10}N_2O_2S$ . The molecular weight is 186.2.

### **DESCRIPTION**

Carbimazole is a white or yellowish-white crystalline powder, slightly soluble in water, soluble in alcohol and in acetone.

NEO-MERCAZOLE is available as a pink tablet containing the following excipients: lactose, sucrose, starch-maize, magnesium stearate, talc, cellulose-microcrystalline, acacia, ferric oxide food grade (77491), propyl hydroxybenzoate and gelatin.

### **PHARMACOLOGY**

NEO-MERCAZOLE is an anti-thyroid agent.

NEO-MERCAZOLE is believed to exert its antithyroid effect by 'blocking' the organic binding of iodine through inhibition of the iodination of tyrosine. It is also thought to have some action on peroxidase which is required as a catalyst in the synthesis of thyroxine by the thyroid gland. It does not affect the uptake of iodine by the thyroid gland and this is of vital importance in the treatment of thyrotoxicosis with radioactive iodine or with a combination of radioiodine and NEO-MERCAZOLE, and also in preparation of patients for operation.

Carbimazole is completely and rapidly metabolised to methimazole and it is the latter that is responsible for the antithyroid activity of carbimazole. Carbimazole is rapidly absorbed from the gastrointestinal tract. The mean peak plasma concentration of methimazole is reported to occur one hour after a single dose of carbimazole. The plasma half-life of methimazole is reported as between 3 and 6 hours. Most of an orally administered dose of carbimazole is excreted in the urine. Less than 12% may be excreted as unchanged methimazole.

### **INDICATIONS**

Therapy of hyperthyroidism. Definitive therapy: induction of a permanent remission, in either primary or secondary thyrotoxicosis. Preparation for thyroidectomy. Before and after radioactive iodine treatment.

## **CONTRAINDICATIONS**

NEO-MERCAZOLE is contraindicated in patients with a previous history of adverse reactions to carbimazole.

Should be given with caution if there is any degree of tracheal obstruction, as high dosage may increase thyroid enlargement and aggravate obstructive symptoms.

## **PRECAUTIONS**

Patients should be warned about the onset of sore throats, mouth ulcers, pyrexia, or other symptoms which might suggest the early development of bone marrow depression. In such cases it is important that drug treatment is stopped and medical advice sought immediately. In such patients, blood cell counts should be performed, particularly where there is any clinical evidence of infection. Early withdrawal of the drug will increase the chance of complete recovery.

NEO-MERCAZOLE should be used with caution in patients with liver disorders.

NEO-MERCAZOLE should be stopped temporarily at the time of administration of radio-iodine.

The use of carbimazole in non-pregnant women of childbearing potential should be based on individual risk/benefit assessment (see Use in Pregnancy).

## **Carcinogenicity, Mutagenicity and Impairment of Fertility**

There is no information on carcinogenicity, mutagenicity or impairment of fertility following treatment with carbimazole.

## **Use in Pregnancy (Category C)**

Antithyroid agents may cause congenital goitre by inhibiting thyroxine synthesis in the foetus. During pregnancy these products should therefore only be used after carefully weighing the mother's needs against the risk to the foetus.

Studies have shown that the incidence of congenital malformations is greater in the children of mothers whose hyperthyroidism has remained untreated than in those who have been treated with carbimazole. However, very rare cases of congenital malformations have been observed following the use of carbimazole or its active metabolite methimazole during pregnancy. A causal relationship of these malformations, especially choanal atresia and aplasia cutis congenital, to transplacental exposure to carbimazole and methimazole cannot be excluded.

The basal metabolic rate is raised during pregnancy and the dosage of NEO-MERCAZOLE must be adjusted accordingly. The smallest dose compatible with rendering the patient symptom free should be employed. The dosage during the last 3 months of pregnancy should, if possible, not exceed 15mg twice daily.

NEO-MERCAZOLE should be discontinued 3 to 4 weeks before delivery and a course of iodine should be substituted. The danger of producing hypothyroid babies as a result of low dosage antithyroid therapy during pregnancy appears to have been grossly exaggerated.

### **Use in Lactation**

Carbimazole and related drugs cross the placenta and are concentrated in the breast milk. Infants should not be breastfed by mothers taking carbimazole.

### **ADVERSE REACTIONS**

All toxic reactions to carbimazole occurred within 8 weeks of starting treatment, and there was no reaction in patients who received 20 mg or less of carbimazole per day. The most common minor side effects are nausea, headache, arthralgia and mild gastric distress. Mild skin rashes can occur and these often respond to antihistamines without discontinuation of the drug. Pruritus and urticaria have been reported. Hair loss has been occasionally reported. Of the major toxic reactions to carbimazole, bone marrow depression is the most serious and can lead to agranulocytosis. Rare cases of pancytopenia/aplastic anaemia, very rare cases of haemolytic anaemia and isolated thrombocytopenia have also been reported.

Hepatic disorders, most commonly jaundice, have been reported; in these cases carbimazole should be withdrawn.

Isolated cases of myopathy were reported in patients complaining from myalgia. Monitoring of creatine kinase (CPK) levels is recommended in these instances.

### **DOSAGE AND ADMINISTRATION**

It is customary to begin therapy with a dosage that will fairly quickly control the thyrotoxicosis and render the patient euthyroid, and later to reduce this.

**Adults:** *Usual initial dosages.* Mild cases, 15 to 20mg/day in divided doses; moderate cases, 30mg/day in divided doses; severe cases, 40 to 45mg (up to 60mg) /day in divided doses.

If large stores of hormone are present, as in nodular goitre, response to NEO-MERCAZOLE may be delayed for several weeks or months, whereas in severe thyrotoxicosis, when very little hormone is stored, improvement may be detected within three to four days.

*Maintenance dosage.* When symptoms are controlled the dosage should be reduced to a maintenance level, which will usually be between 10 and 15mg daily.

Experience has shown there is a wide variation of sensitivity to the drug from time to time in a particular patient. For this reason, patients should be seen monthly for the first year; and thereafter at 3 or 6 monthly intervals. Once a remission has been secured, maintenance dosage should be continued for at least 12 months, and up to 2 years of treatment may be required.

If thyroidectomy is intended, it can be carried out once the euthyroid state is achieved with NEO-MERCAZOLE, which is then discontinued.

*Changeover from thiouracils:* When treatment with one of the thiouracils is replaced by NEO-MERCAZOLE therapy, 50mg of methylthiouracil or propylthiouracil can be taken as equivalent to 5mg of NEO-MERCAZOLE.

*Delayed Response to NEO-MERCAZOLE Therapy:* If no relief is obtained within three months, the possible causes are: patients have failed to take their NEO-MERCAZOLE (this is the most

common cause); previous iodine therapy which has resulted in an increased hormone store within the gland; inadequate dosage of NEO-MERCAZOLE.

*Preparation of Thyrotoxic Patients for Surgery:* NEO-MERCAZOLE is prescribed prior to thyroidectomy and should then be given in sufficient dosage and for long enough to render the patient euthyroid. It should be continued up to the time of operation but should be prescribed together with iodide during the last 2 weeks.

### **OVERDOSAGE**

**Symptoms:** The principle manifestations of poisoning are skin rash and leucopenia. Acute poisoning has not been reported.

**Treatment:** Treat toxic neuropathy by physiotherapy.

### **STORAGE**

Store below 30°C. Protect from moisture.

### **PRESENTATION**

NEO-MERCAZOLE is available for oral administration as a pink circular biconvex tablet in a 5mg strength. Each tablet is scored.

NEO-MERCAZOLE is available in a bottle of 100 tablets.

### **DISTRIBUTOR**

Link Medical Products Pty Ltd

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**Date of Most Recent Amendment: October 23, 2007**