

Data Sheet

Neo-Mercazole®

Carbimazole 5mg tablet

Anti-thyroid agent

Qualitative and Quantitative Composition

Active Ingredient

Each Neo-Mercazole tablet contains carbimazole 5mg.

Excipients

Lactose, maize starch, sucrose, magnesium stearate, talc, gum acacia, ferric oxide, gelatin.

Pharmaceutical Form

A pale pink tablet, shallow bi-convex tablet with a white centrally located core, one face plain, with Neo 5 imprinted on the other.

Clinical Particulars

Therapeutic Indications

Primary thyrotoxicosis, even in pregnancy.

Secondary thyrotoxicosis - toxic nodular goitre.

However, Neo-Mercazole really has three principal applications in the therapy of hyperthyroidism:

1. Definitive therapy - induction of a permanent remission.
2. Preparation for thyroidectomy.
3. Before and after radio-active iodine treatment.

Posology and Method of Administration

Neo-Mercazole should only be administered if hyperthyroidism has been confirmed by laboratory tests.

Adults

Initial dosage

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

The usual initial dosage for adults is up to 60 mg per day given in divided doses. Thus:

Mild cases	20 mg	Daily in divided
Moderate cases	40 mg	

Severe cases	40-60 mg	dosage.
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The initial dose should be titrated against thyroid function until the patient is euthyroid in order to reduce the risk of over-treatment and resultant hypothyroidism.

Three factors determine the time that elapses before a response is apparent:

- (a) The quantity of hormone stored in the gland.
(Exhaustion of these stores usually takes about a fortnight).
- (b) The gland secretory rate.
- (c) The degree of inhibition of hormone synthesis achieved by Neo-Mercazole.

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 15 mg daily which may be taken as a single daily dose.

Experience has shown there is a wide variation of sensitivity to the medicine and from time to time in a particular patient. For this reason patients should be seen monthly for the first year; and thereafter at three or six-monthly intervals.

Serial thyroid function monitoring is recommended, together with appropriate dosage modification in order to maintain a euthyroid state.

Elderly

No special dosage regimen is required, but care should be taken to observe the contraindications and warnings as it has been reported that the risk of a fatal outcome to neutrophil dyscrasia may be greater in the elderly (aged 65 or over).

Children

The usual initial daily dose is 15 mg per day.

Duration of therapy

First, the time required to render a patient euthyroid depends very much on the type of case being treated. Toxic nodular goitres usually take very much longer.

Second, once a remission has been secured maintenance dosage should be continued for at least twelve months, and up to two years of Neo-Mercazole treatment may be required.

Of course, if thyroidectomy is intended, it can be carried out once the euthyroid state is achieved with Neo-Mercazole, which is then discontinued.

Change-over from thiouracils

When treatment with one of the thiouracils is replaced by Neo-Mercazole therapy, one 50 mg tablet of methylthiouracil or propylthiouracil can be taken as equivalent to one 5 mg tablet of Neo-Mercazole.

Delayed response to therapy

If no relief is obtained within three months, the possible causes are:

- (a) Patients have failed to take their Neo-Mercazole. This is the most common cause.
- (b) Previous iodine therapy which has resulted in an increased hormone store within the gland.
- (c) 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 for long enough to render the patient euthyroid.

Contraindications

Neo-Mercazole is contraindicated in patients with:

- a previous history of adverse reactions to carbimazole or to any of the excipients in the composition
- serious, pre-existing haematological conditions
- **severe** hepatic insufficiency.

Special Warnings and Special Precautions for Use

As fatal cases of agranulocytosis with carbimazole have been reported and early treatment of agranulocytosis is essential, it is important that patients should always be warned about the onset of sore throats, bruising or bleeding, mouth ulcers, fever, malaise and should be instructed to stop the drug and to seek medical advice immediately. In such patients, blood cell counts should be performed immediately, particularly where there is any clinical evidence of infection. Early withdrawal of Neo-Mercazole will increase the chance of complete recovery.

Following the onset of any signs and symptoms of hepatic disorder (pain in the upper abdomen, anorexia, general pruritus) in patients, the drug should be stopped and liver function tests performed immediately.

Neo-Mercazole should be used with caution in patients with mild-moderate hepatic insufficiency. If abnormal liver function is discovered, the treatment should be stopped. The half-life may be prolonged due to the liver disorder.

Neo-Mercazole should be stopped temporarily at the time of administration of radio-iodine.

Patients unable to comply with the instructions for use or who cannot be monitored regularly should not be treated with Neo-Mercazole.

Regular full blood count checks should be carried out in patients who may be confused or have a poor memory.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Precaution should be taken in patients with intrathoracic goitre, which may worsen during initial treatment with Neo-Mercazole. Tracheal obstruction may occur due to intrathoracic goitre.

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

There is a risk of cross-allergy between carbimazole, thiamazole and propylthiouracil.

Interaction with Other Medicinal Products and Other Forms of Interaction

Little is known about interactions.

Particular care is required in case of concurrent administration of medication capable of inducing agranulocytosis. Since carbimazole is a vitamin K antagonist, the effect of anticoagulants could be intensified.

The serum levels of theophylline can increase and toxicity may develop if hyperthyroidic patients are treated with antithyroid medications without reducing the theophylline dosage.

Pregnancy and Lactation

Category C

Carbimazole crosses the placenta but, provided the mother's dose is within the standard range, and her thyroid status is monitored, there is no evidence of neonatal thyroid abnormalities. Studies have shown that the incidence of congenital malformations is greater in the children of mothers whose hyperthyroidism has remained untreated than in those to whom treatment with carbimazole has been given. 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 congenita, to transplacental exposure to carbimazole and methimazole cannot be excluded. Therefore, the use of carbimazole in non-pregnant women of childbearing potential should be based on individual risk/benefit assessment (see Special Warnings and Special Precautions for Use). Cases of renal, skull, cardiovascular congenital defects, exomphalos, gastrointestinal malformation, umbilical malformation and duodenal atresia have also been reported. Therefore, carbimazole should be used in pregnancy only when propylthiouracil is not suitable. If Neo-Mercazole is used in pregnancy the dose of Neo-Mercazole must be regulated by the patient's clinical condition. The lowest dose possible should be used, and this can often be discontinued three to four weeks before term, in order to reduce the risk of neonatal complications. The blocking-replacement regimen should not be used during pregnancy since very little thyroxine crosses the placenta in the last trimester.

Neo-Mercazole is secreted in breast milk and, if treatment is continued during lactation, the patient should not continue to breast-feed her baby.

Effects on Ability to Drive and Use Machines

The effect on the ability to drive and use machines is not known.

Undesirable Effects

Adverse reactions usually occur in the first eight weeks of treatment. The most frequently occurring reactions are nausea, headache, arthralgia, mild gastric distress, skin rashes and pruritus. These reactions are usually self-limiting and may not require withdrawal of the medicine.

Blood and lymphatic system disorders

Bone marrow depression including neutropenia, eosinophilia, leukopenia, agranulocytosis has been reported. Fatalities with carbimazole-induced agranulocytosis have been reported. Rare cases of pancytopenia/aplastic anaemia and isolated thrombocytopenia have also been reported. Additionally, very rare cases of haemolytic anaemia have been reported.

Patients should always be warned about the onset of sore throats, bruising or bleeding, mouth ulcers, fever, malaise and should be instructed to stop the medicine and to seek medical advice immediately. In such patients, blood cell counts should be performed **immediately**, particularly where there is any clinical evidence of infection.

Nervous system disorders

Headache

Gastro-intestinal system disorders

Nausea, mild gastric distress. Loss of sense of taste has been observed.

General disorders and administration site conditions

Fever, Malaise

Hepato-biliary system disorders

Hepatic disorders, including abnormal liver function tests, hepatitis, cholestatic hepatitis, cholestatic jaundice and mostly commonly jaundice, have been reported; in these cases carbimazole should be withdrawn.

Injury, poisoning and procedural complications

Bruising

Skin and subcutaneous tissue disorders

Skin rashes, pruritis, urticaria. Hair loss has been occasionally reported.

Musculoskeletal system disorders

Isolated cases of myopathy have been reported. Patients experiencing myalgia after the intake of Neo-Mercazole should have their creatine phosphokinase levels monitored.

Hypersensitivity and allergic reaction

Angioedema and multi-system hypersensitivity reactions such as cutaneous vasculitis, liver, lung and renal effects occur.

Vascular Disorders

Bleeding

Overdosage

No symptoms are likely from a single large dose, and so no specific treatment is indicated.

Pharmacological Properties***Pharmacodynamic Properties***

Carbimazole is a thyroid reducing agent.

Pharmacokinetic Properties

Carbimazole is rapidly metabolised to methimazole. The mean peak plasma concentration of methimazole is reported to occur one hour after a single dose of carbimazole. The apparent plasma half-life of methimazole is reported as 6.4 hours.

Preclinical Safety Data

Not relevant.

Pharmaceutical Particulars

Incompatibilities

None known.

Shelf Life

Neo-Mercazole should not be used beyond the expiry date printed on the pack.

Special Precautions for Storage

Store at or below 25 °C in a dry place. Store in the original container.

Nature and Contents of Container

Neo-Mercazole 5mg tablets are available in HDPE containers with an LDPE closure. Each bottle contains 100 tablets.

Instructions for Use/Handling

No special requirements.

Medicine Classification

Prescription medicine.

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Date of Preparation

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