

APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

BIROIDA tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains 5 mg of carbimazole.

Contains sugar: lactose anhydrous 70 mg per tablet.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Uncoated tablet.

White coloured, round shaped, uncoated tablets, debossed "5" on one side and break line on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

BIROIDA is indicated in the management of hyperthyroidism, thyrotoxicosis (including thyroid storm), and also for the preparation of patients for thyroidectomy.

BIROIDA can also be used for therapy prior to and post radio-active ablative therapy.

4.2 Posology and method of administration

Posology

BIROIDA should only be administered if hyperthyroidism has been confirmed by laboratory tests.

10 mg to 60 mg daily according to the severity of the disorder. The dose should be gradually reduced to the smallest amount which will control the disease.

Daily dosage should be divided and titrated against thyroid function until the patient is euthyroid in order to reduce the risk of over-treatment and resultant hypothyroidism.

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

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to carbimazole, other thiourea antithyroid medicines, or to any of the excipients (see section 6.1).
- Serious, pre-existing haematological conditions.
- Severe hepatic insufficiency.
- Patients with a history of acute pancreatitis after administration of carbimazole or its active metabolite thiamazole.
- Tracheal obstruction.

4.4 Special warnings and precautions for use

Bone marrow depression including neutropenia, eosinophilia, leucopenia and agranulocytosis has been reported. Fatalities with carbimazole-induced agranulocytosis have been reported.

Cases of pancytopenia/aplastic anaemia and isolated thrombocytopenia have also been reported. Additionally, cases of haemolytic anaemia have been reported.

Patients should always be warned about the onset of sore throats, bruising or bleeding, mouth

ulcers, fever and malaise and should be instructed to stop BIROIDA and to seek medical advice immediately. In such patients, white blood cell counts should be performed immediately, particularly where there is any clinical evidence of infection.

There have been post-marketing reports of acute pancreatitis in patients receiving carbimazole or its active metabolite thiamazole. In case of acute pancreatitis, BIROIDA should be discontinued immediately. BIROIDA must not be given to patients with a history of acute pancreatitis after administration of carbimazole or its active metabolite thiamazole. Re-exposure may result in recurrence of acute pancreatitis, with decreased time to onset.

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

Early withdrawal of BIROIDA will increase the chance of complete recovery.

BIROIDA 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.

BIROIDA should be stopped temporarily at the time of administration of radio-iodine (to avoid thyroid crisis).

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

Regular full blood count checks should be carried out in patients who may be confused or

have a poor memory.

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

There is a risk of cross-allergy between carbimazole, the active metabolite thiamazole (methimazole) and propylthiouracil.

Women of childbearing potential and pregnancy

Women of childbearing potential have to use effective contraceptive measures during treatment. If BIROIDA is used during pregnancy, the lowest effective dose without additional administration of thyroid hormones should be administered. Close maternal, foetal and neonatal monitoring is warranted (see section 4.6).

Lactose

BIROIDA contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with the rare hereditary conditions of galactose intolerance, total lactase deficiency, glucose-galactose malabsorption should not take BIROIDA.

4.5 Interaction with other medicines and other forms of interaction

Particular care is required in case of concurrent administration of medicine capable of inducing agranulocytosis.

Since BIROIDA is a vitamin K antagonist, the effect of anticoagulants could be intensified. Additional monitoring of prothrombin time/international normalised ratio (PT/INR) should be considered, especially before surgical procedures.

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

Co-administration of prednisolone and BIROIDA may result in increased clearance of prednisolone.

BIROIDA may inhibit the metabolism of erythromycin, leading to reduced clearance of erythromycin.

Serum digoxin levels may be increased when hyperthyroid patients on a stable digoxin regimen become euthyroid; a reduced dosage of digoxin may be needed.

Hyperthyroidism may cause an increased clearance of beta-adrenergic blockers with a high extraction ratio. A dose reduction of beta blockers may be needed when a hyperthyroid patient becomes euthyroid.

Laboratory value alterations

With diagnostic test results:

BIROIDA may decrease thyroidal uptake of sodium iodide I 123 or I 131, or pertechnetate, withdrawal of BIROIDA 5 days or more before radioactive iodine uptake tests is necessary to prevent interference.

With physiology laboratory test values:

Alanine aminotransferase (ALT [SGPT]) serum concentrations, alkaline phosphatase serum concentrations, aspartate aminotransferase (AST [SGOT]) serum concentrations, bilirubin serum concentrations, lactate dehydrogenase (LDH) serum concentrations and prothrombin time (PT) may be increased, and may indicate hepatotoxicity and be associated with

splenomegaly.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential have to use effective contraceptive measures during treatment (see section 4.4).

Pregnancy

Safety in pregnancy and lactation has not been established. BIROIDA may cause foetal or neonatal hypothyroidism and goitre. BIROIDA 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.

Cases of congenital malformations have been observed following the use of BIROIDA or its active metabolite methimazole during pregnancy. A causal relationship of these malformations, especially choanal atresia and aplasia cutis congenital, to transplacental exposure to BIROIDA and methimazole cannot be excluded. Therefore, the use of BIROIDA in non-pregnant women of childbearing potential should be based on individual risk/benefit assessment. Cases of renal, skull, cardiovascular congenital defects, exomphalos, gastrointestinal malformation, umbilical malformation and duodenal atresia have also been reported.

Lactation

BIROIDA is excreted in milk and if treatment is continued during lactation the patient should not continue to breastfeed her baby.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

a. Summary of the safety profile

Adverse reactions usually occur in the first eight weeks of treatment.

The most frequent minor reactions are nausea, headache, arthralgia, mild gastrointestinal disturbance, skin rashes and pruritus. These reactions are usually self-limiting and may not require withdrawal of the medicine.

b. Tabulated summary of adverse reactions

The undesirable effects are listed below by system organ class. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness

| MedDRA system organ class | Frequency | Adverse reactions |
|--------------------------------------|-------------------|--|
| Blood and lymphatic system disorders | Less frequent | Bone-marrow depression including neutropenia, eosinophilia, leukopenia. Fatalities with carbimazole-induced, agranulocytosis have been reported (see section 4.4). |
| | Frequency unknown | Pancytopenia/aplastic anaemia, thrombocytopaenia, haemolytic anaemia |
| Immune system disorders | Less frequent | Angioedema, multi-system hypersensitivity reactions such as cutaneous vasculitis, liver, lung and renal effects |
| Endocrine disorders | Frequency unknown | Insulin autoimmune syndrome (with pronounced decline in blood glucose level) |

| MedDRA system organ class | Frequency | Adverse reactions |
|--|-------------------|---|
| Nervous system disorders | Frequent | Headache |
| | Frequency unknown | Paraesthesias, neuritis, polyneuropathy |
| Vascular disorders | Frequency unknown | Vassculitis, bleeding |
| Gastrointestinal disorders | Frequent | Gastrointestinal disturbances (including nausea, vomiting and gastric discomfort) |
| | Frequency unknown | Taste disturbances, acute salivary gland swelling, acute pancreatitis |
| Hepato-biliary disorders | Less frequent | Jaundice, abnormal liver function tests, hepatitis, cholestatic jaundice; in these cases of hepatic disorder BIROIDA should be withdrawn and not re-introduced. |
| Skin and subcutaneous tissue disorders | Frequent | Rash, pruritus, skin pigmentation, urticaria |
| | Less frequent | Severe cutaneous hypersensitivity reactions, including Stevens-Johnson syndrome (very rare including isolated reports: severe forms, including generalised dermatitis, have only been described in isolated cases). |
| | Frequency | Abnormal hair loss |

| MedDRA system organ class | Frequency | Adverse reactions |
|--|-------------------|---|
| | unknown | |
| Musculoskeletal and connective tissue disorders | Less frequent | Myopathy, arthralgia. Patient experiencing myalgia after the intake of BIROIDA should have their creatine phosphokinase levels monitored. |
| | Frequency unknown | Lupus-like syndrome |
| Renal and urinary disorders | Frequency unknown | Nephritis |
| General disorders and administration site conditions | Frequency unknown | Fever, malaise |
| Injury, poisoning and procedural complications | Frequency unknown | Bruising |

Paediatric population

Frequency, type and severity of adverse reactions in children appear to be comparable with those in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “**6.04 Adverse Drug Reactions Reporting Form**”, found online under SAHPRA’s publications:

<https://www.sahpra.org.za/Publications/Index/8>

4.9 Overdose

Signs and symptoms

Overdosage or accidental poisoning may result in hypothyroidism and goitre. If blood dyscrasias occur, the medicine should be withdrawn immediately

Management of overdose

Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sulfur-containing imidazole derivatives.

ATC Code: H03BB01

A.21.3 Thyroid preparations

Carbimazole is an anti-thyroid medicine which depresses the formation of thyroid hormone. It reduces the uptake and concentration of inorganic iodine by the thyroid, but its main effect is to reduce the formation of di-iodotyrosine and thyroxine.

5.2 Pharmacokinetic properties

Absorption

Carbimazole is rapidly metabolised to thiamazole. After oral ingestion, peak plasma concentrations of thiamazole, the active moiety, occur at 1 to 2 hours.

Distribution

The total volume of distribution of thiamazole is 0,5 l/kg. Thiamazole is concentrated in the thyroid gland. This intrathyroidal concentration of thiamazole has the effect of prolonging its activity. However, thiamazole has a shorter half-life in hyperthyroid patients than in normal controls and so more frequent initial doses are required while the hyperthyroidism is active.

Biotransformation

Thiamazole is moderately bound to plasma proteins. Carbimazole has a half-life of 5,3 to 5,4 hours. It is possible that the plasma half-life may also be prolonged by renal or hepatic disease (see section 4.2). Thiamazole crosses the placenta and appears in breast milk. The plasma: milk ratio approaches unity.

Elimination

Over 90 % of orally administered carbimazole is excreted in the urine as thiamazole or its metabolites. The remainder appears in faeces. There is 10 % enterohepatic circulation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium

Lactose anhydrous

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C. Protect from moisture.

Keep in the original container until required for use.

6.5 Nature and contents of container

PVC/PE/PVDC/Aluminium foil blisters in brown coloured cartons of 20, 28, 30, 50, 56, 100 and 112 pack sizes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special precautions are required.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Strides Pharma SA (Pty) Ltd

106 16th Road

Building 2

Midrand

South Africa

1686

8 REGISTRATION NUMBER

BIROIDA 54/21.3/0149

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 July 2023

10 DATE OF REVISION OF THE TEXT