SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Carbimazole 5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains Carbimazole Ph. Eur. 5mg
Each tablet also contains lactose monohydrate. For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Tablet
White, round, biconvex, uncoated tablets with a score line on one side and embossed ‘F1’ on the other

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Carbimazole is an anti-thyroid agent. It is indicated in all conditions where reduction of thyroid function is required.
1. Hyperthyroidism.
2. Preparation for thyroidectomy in hyperthyroidism.
3. Preparation for, and as concomitant therapy with, radio-iodine treatment.

4.2 Posology and method of administration
Carbimazole should only be administered if hyperthyroidism has been confirmed by laboratory tests

Adults
The initial dose is in the range 20 - 60mg and should be titrated against thyroid function until the patient is euthyroid in order to reduce the risk of overtreatment and resultant hypothyroidism. Subsequent therapy may then be administered in one of two ways.

Maintenance regimen: Final dosage is usually in the range 5 - 15mg per day, which may be taken as a single daily dose. Therapy should be continued for at least six, and up to 18 months. Serial thyroid function monitoring is recommended, together with appropriate dosage modification in order to maintain a euthyroid state.

Blocking-replacement regimen: Dosage is maintained at the initial level, i.e. 20 - 60mg per day, and supplemental l-thyroxine, 50 - 150mcg per day, is
administered concomitantly, in order to prevent hypothyroidism. Therapy should be continued for at least six months, and up to eighteen months. Where a single dosage of less than 20mg is recommended, it is intended that Carbimazole 5mg Tablets should be taken.

**Elderly**

No special dosage regimen is required, but care should be taken to observe the contra-indications and warnings.

**Children**

The usual initial daily dose is 15mg per day.

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### 4.3 Contraindications

Carbimazole is contra-indicated 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.

### 4.4 Special warnings and 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.

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.

Early withdrawal of the drug will increase the chance of complete recovery. Carbimazole 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. Carbimazole 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 carbimazole.

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 carbimazole. 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 section 4.6). There is a risk of cross-allergy between carbimazole, thiamazole and propylthiouracil.
4.5 **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 patients are treated with antithyroid medications without reducing the theophylline dosage.

4.6 **Pregnancy and lactation**

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 section 4.4). 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 carbimazole is used in pregnancy the dose of carbimazole 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. Carbimazole is secreted in breast milk and, if treatment is continued during lactation, the patient should not continue to breast-feed 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**

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 drug.

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

**Blood and lymphatic system disorders**
Bone marrow depression including neutropenia, eosinophilia, leukopenia, and 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 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.
Generalised lymphadenopathy.

**Endocrine disorders**
Insulin autoimmune syndrome (with pronounced decline in blood glucose level).

**Nervous system disorders**
Headache, neuritis, polyneuropathy.

**Gastro-intestinal system disorders**
Nausea, mild gastric distress. Loss of sense of taste has been observed.
Acute salivary gland swelling.

**General disorders and administration site conditions**
Fever, Malaise

**Hepatobiliary disorders**
Hepatic disorders, including abnormal liver function tests, hepatitis, cholestatic hepatitis, cholestatic jaundice and most 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, pruritus, urticaria. Hair loss has been occasionally reported.
Severe cutaneous hypersensitivity reactions have been reported in both adult and paediatric patients, including Stevens-Johnson syndrome (very rare including isolated reports: severe forms, including generalised dermatitis, have only been described in isolated cases).

**Musculoskeletal and connective tissue disorders**
Isolated cases of myopathy have been reported. Patients experiencing myalgia after the intake of carbimazole should have their creatine phosphokinase levels monitored.
**Immune system disorders**
Angioedema and multi-system hypersensitivity reactions such as cutaneous vasculitis, liver, lung and renal effects occur.

**Vascular Disorders**
Bleeding

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme (Website: www.mhra.gov.uk/yellowcard).

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

5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**
Carbimazole is a thyroid reducing agent. ATC code: H03BB01

5.2 **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.

5.3 **Preclinical safety data**
Not relevant.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**
Lactose monohydrate
Maize Starch
Citric acid monohydrate
Magnesium stearate
6.2 **Incompatibilities**
Not applicable

6.3 **Shelf life**
36 months

6.4 **Special precautions for storage**
Do not store above 25°C. Store in original container. Keep the container tightly closed

6.5 **Nature and contents of container**
Tablets are packed in a PP or HDPE container with child resistant cap (built in 2gm silica gel) containing 100 tablets.

6.6 **Special precautions for disposal**
No special requirements.

7 **MARKETING AUTHORISATION HOLDER**

Lime Pharma Limited
Whiddon Valley,
Barnstaple,
North Devon,
EX32 8NS,
United Kingdom.

8 **MARKETING AUTHORISATION NUMBER(S)**
PL 20620/0005

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
18/02/2008

10 **DATE OF REVISION OF THE TEXT**
04/08/2016