SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Propylthiouracil 50 mg Tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of propylthiouracil.

Excipient with known effect:

Each tablet contains 33.5 mg of lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

White, circular biconvex tablet of approximately 6.5 mm by 3 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Propylthiouracil 50 mg Tablets is indicated in adults (including the elderly), children and adolescents aged 6 to 18 years, for the treatment of hyperthyroidism.

4.2 Posology and method of administration

Posology

Adults, including the elderly

Initially 300 to 600 mg daily, once daily or in divided doses until the patient becomes euthyroid.

When the condition is controlled (usually after 1-2 months), the dose is reduced to 50 to 150 mg daily and continued for 1-2 years.

Patients with renal failure

GFR 10 to 50 ml/min, 75% dose.

GFR < 10 ml/min, 50% dose.

Patients with hepatic disease

Reduced dose.

Paediatric population

Children under 6 years of age: Propylthiouracil 50 mg Tablets should not be used in children under 6 years of age because of safety concerns.

Children aged 6 to 10 years: Initially 50 to 150 mg once daily or in divided doses.

Children aged over 10 years: Initially 150 to 300 mg once daily or in divided doses.

Method of administration

Oral use.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Previous severe hypersensitivity reaction e.g. agranulocytosis, hepatitis, vasculitis and nephritis with propylthiouracil.

4.4 Special warnings and precautions for use

Due to the risk of agranulocytosis it is advised that patients should be warned to report to their doctor in the event of a sore throat, fever, mouth ulcers, bruising, malaise, non-specific illness or other symptoms of infection immediately. A full blood count should be performed and treatment should be discontinued immediately if there is clinical or laboratory evidence of neutropenia.

The prothrombin time should be monitored during therapy, especially prior to surgery, because propylthiouracil may cause thrombocytopenia.

Hepatic and renal impairment

Some cases of severe hepatic reactions, both in adults and children, including fatal cases and cases requiring a liver transplant have been reported with propylthiouracil. Time to onset has varied but in a majority of cases the liver reaction occurred within six months. If significant hepatic enzyme abnormalities develop during treatment with propylthiouracil the medicine should be discontinued immediately (see section 4.8).

Propylthiouracil should be used with caution in patients with renal impairment or hepatic disease (see section 4.2). Patients should be advised of the symptoms of hepatic dysfunction (anorexia, pruritis, right upper quadrant pain etc.) and told to report them immediately. The occurrence of hepatic necrosis may have fatal consequences (see section 4.8).

Intolerance to sugars

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

Regular monitoring of the thyroid function (thyroid hormone tests and TSH) is required during therapy with antithyroid agents to avoid overdosing (see section 4.9).

4.5 Interaction with other medicinal products and other forms of interaction

Drug induced changes in thyroid status may affect the dosage requirements for theophylline, digoxin or beta-blockers. The doses of theophylline, digoxin or beta-blockers may need to be reduced as thyroid function returns to normal.

Pre-treatment with propylthiouracil may reduce the effectiveness of radio-iodine (^{131}I) therapy for hyperthyroidism. This is supported by four studies one of which, a randomised study in 80 patients, showed an approximate halving of cure rate one year after ^{131}I therapy in patients pre-treated with propylthiouracil.

4.6 Fertility, pregnancy and lactation

Pregnancy

Propylthiouracil may be given in pregnancy. It crosses the placenta and in high doses may cause foetal goitre and hypothyroidism, therefore the lowest possible dose should be given and thyroid function monitored every four to six weeks to maintain optimum control.

Breast-feeding

Propylthiouracil also transfers to breast milk, reaching about 10% of the serum concentration, but this does not preclude breast-feeding. Neonatal development and infant thyroid function should be closely monitored. The lowest effective dose should be used.

Fertility

Males

Hyperthyroidism can cause a marked reduction in sperm count resulting in infertility. Treatment with propylthiouracil may result in normalisation in sperm count once the thyroid function is controlled.

Women of childbearing potential

Hyperthyroidism can cause a reduction in fertility. Treatment with propylthiouracil can result in rapid normalisation in fertility once the thyroid function is controlled.

4.7 Effects on ability to drive and use machines

Propylthiouracil 50 mg tablets has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Blood and lymphatic system disorders

Reversible leucopenia. Rarely, agranulocytosis, thrombocytopenia, leucopenia, aplastic anaemia, pancytopenia. A rare complication of therapy is a tendency to haemorrhage associated with hypoprothrombinaemia which may be controlled by the administration of phytomenadione.

Immune system disorders

Interstitial pneumonitis, alveolar haemorrhage, lymphadenopathy, arthritis, nephritis, vasculitis and lupus erythematosus-like syndromes have occurred in some patients taking thiourea antithyroid drugs. An immune mechanism has been proposed. There have also been rare reports of acute glomerulonephritis. Hypersensitivity reactions may also be associated with the development of antineutrophil cytoplasmic antibodies (ANCA).

Nervous system disorders

Headache.

Ear and labyrinth disorders

Rarely, hearing impairment may occur with propylthiouracil. The impairment usually becomes less marked after withdrawal of the drug.

Gastrointestinal disorders

Nausea, gastrointestinal disturbances, taste perversion. Rarely vomiting.

Hepatobiliary disorders

Jaundice (usually cholestatic), hepatic necrosis (sometimes with fatal consequences), encephalopathy. More commonly, asymptomatic liver function test abnormalities (increased serum bilirubin, Alanine transaminase and / or alkaline phosphatase concentrations), which are reversible on dose reduction or discontinuation of treatment, may occur with propylthiouracil.

Frequency unknown: Hepatitis, hepatic failure.

Skin and subcutaneous tissue disorders

Mild papular skin rashes, pruritus, urticaria, alopecia, cutaneous vasculitis.

Musculoskeletal and connective tissue disorders

Myopathy, arthralgia.

General disorders and administration site conditions

Fever.

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 national reporting system listed in Appendix V.

4.9 Overdose

Symptoms

Goitre and hypothyroidism may be induced by repeated over dosage. Single overdose is not dangerous. Overdose may manifest as vomiting, epigastric distress, headache, fever, arthralgia, pruritis and pancytopenia.

Management

The treatment of propylthiouracil overdose should aim to minimise the amount of drug absorbed in the circulation. Treatment should involve liberal use of oral fluids. Activated charcoal may also be employed. General symptomatic and supportive measures should then be instituted. A full blood analysis should be considered because of the slight risk of haematological complications and appropriate therapy given if bone marrow depression develops.

There is no specific antidote for propylthiouracil.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Thyroid therapy. ATC Code: H03BA02

Mechanism of action

Propylthiouracil is an antithyroid drug that depresses the formation of thyroid hormone. This is effected by interference both with the incorporation of iodine into tyrosyl residues and the coupling of such residues to form iodothyronines. Propylthiouracil achieves these actions by the inhibition of the enzyme peroxidase.

Pharmacodynamic effects

Its effects are only manifested after a latent period of up to 3 to 4 weeks because all the preformed hormone has to be used up before circulatory concentrations will fall.

5.2 Pharmacokinetic properties

Absorption

Propylthiouracil is rapidly absorbed from the gut with average peak blood levels about one hour after administration of an oral dose. Between half and three quarters of the oral dose is bioavailable due to incomplete absorption or rapid first pass metabolism by the liver.

Distribution

Plasma half-life is 1-3 hours, the volume of distribution approximately 30 l with about 80% plasma binding.

Elimination

Most is excreted as the glucuronic acid conjugate in the urine.

5.3 Preclinical safety data

There have been no systematic long term animal toxicology studies performed. Some short term studies carried out when this class of drugs was introduced show that rats and rodents treated with high doses of propylthiouracil and made markedly hypothyroid will frequently develop thyroid hyperplasia, adenomas, carcinoma, pituitary adenomas and parathyroid hyperplasia.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Acacia, spray-dried

Croscarmellose sodium

Sodium laurilsulfate

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in the original package in order to protect from light.

6.5 Nature and contents of container

White polypropylene bottles fitted with a tamper evident high density polyethylene (HDPE) cap containing 100 tablets.

Opaque PVC/PVDC aluminium foil blister containing 14 tablets. Two or four blisters are provided per pack (28 or 56 tablets).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Halewood Chemicals Limited,
The Mill, Horton Road, Stanwell Moor,
Staines, Middlesex, TW19 6BJ, UK.

8. MARKETING AUTHORISATION NUMBER(S)

PL 00042/0205

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/12/2016

10. DATE OF REVISION OF THE TEXT

22/12/2016