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 31.8 mg of lactose (as monohydrate).
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
Due to individual variability in absorption rates, the dosage should be based on prior measurement of thyroid hormone levels. The lowest possible effective dose should be used to avoid the risk of hypothyroidism (see Section 4.4).
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 or hepatic impairment:
Renal and liver function should always be tested before starting therapy with Propylthiouracil 50 mg Tablets.

- *Patients with renal impairment*

The dose should be adjusted according to the glomerular filtration rate (GFR), as follows:

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

GFR < 10 ml/min, 50% dose.

- *Patients with hepatic impairment*

A reduced dose should be considered for patients with impaired liver function. *Paediatric population*

Children under 6 years of age: The safety of propylthiouracil in children aged under 6 years has not been established

Children aged six to ten years should receive an initial dose of 50 to 150 mg once daily or in divided doses. Children aged over 10 years and adolescents should receive an initial dose of 150 to 300 mg once daily or in divided doses.

Maintenance dose is determined by the patient's response.

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.

4.4 Special warnings and precautions for use

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)
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, pruritus, 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, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Sodium content
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

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

Hyperthyroidism in pregnant women should be adequately treated to prevent serious maternal and foetal complications.
Propylthiouracil is able to cross the human placenta.
Some epidemiological studies indicate that propylthiouracil use during pregnancy is associated with a slight increased risk of congenital malformations in comparison to women without hyperthyroidism, while others do not support this association. However, the risk appears to be comparable in magnitude to that observed in women with untreated overt hyperthyroidism. Individual benefit/risk assessment is necessary before treatment with propylthiouracil during pregnancy. Propylthiouracil should be administered during pregnancy at the lowest effective dose without additional administration of thyroid hormones. If propylthiouracil is used during pregnancy, close maternal, foetal and neonatal monitoring is recommended.

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

Women of childbearing potential should be informed about the potential risks of propylthiouracil use during pregnancy.

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

The frequency categories for each adverse drug reaction include: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000. <1/1,000); very rare (<1/10,000); or not known (cannot be estimated from the available data).

MedDRA System Organ Class	**Adverse reactions – preferred term**					
	Very common ([3]1/10)	**Common ([3]1/100 to <1/10)**	**Uncommon ([3]1/1 000 to <1/100)**	**Rare ([3]1/10 000 to <1/1 000)**	**Very rare (<1/10 000)**	**not known (cannot be estimated from the available data)**
Blood and lymphatic system disorders		Leukopenia, Neutropenia	Aplastic Anaemia, Agranulocytosis Granulocytopenia, Thrombocytopenia	Hypoprothrombinaemia, Lymphadenopathy, Pancytopenia	Abnormal Erythrocytes, Haemolysis	
Immune system disorders						Hypersensitivity, Polymyositis
Nervous system disorders			Headache	Dizziness Paraesthesia		
Eye disorders						
Ear and labyrinth disorders				Hearing Impairment		
Vascular disorders			Bleeding Vasculitis	Periarteritis		
Respiratory,				Interstitial Pneumonia Interstitial Pneumonitis	Asthma	Pulmonary Haemorrhage

thoracic and mediastinal disorders						
Gastrointestinal disorders		Gastrointestinal Disturbances, Nausea, Taste Disturbances, Vomiting	Stomach Pain			Sialoadenitis
Hepatobiliary disorders			Liver disorders (reversible on discontinuation of treatment) with symptoms such as hepatitis, jaundice and hepatomegaly	Jaundice		Liver Failure
Skin and subcutaneous tissue disorders	Urticaria	Rash		Allergic Vasculitis, Alopecia, Systemic Lupus Erythematosus		Skin Pigmentation
Musculoskeletal and connective tissue disorders				Backache, Neuromuscular Disturbances	Arthralgia	Myalgia, Myopathy
Renal and urinary disorders				Glomerulonephritis Nephritis Renal Vasculitis	Acute Renal Failure	
General disorders and administration site conditions	Pyrexia			Peripheral Oedema		Oedema
Investigations		Abnormal Liver Function Tests				Antineutrophil Cytoplasmic Antibodies (ANCA)

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 HPRA Pharmacovigilance. Website: www.hpra.ie

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

4 years.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions 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 10 or 14 tablets. Packs contain either 28, 56 or 100 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Halewood Pharma Limited
Unit 3D North Point House
North Point Business Park
New Mallow Road
Cork
Republic of Ireland

8 MARKETING AUTHORISATION NUMBER

PA22902/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th February 2017
Date of last renewal: 15th December 2021

10 DATE OF REVISION OF THE TEXT

August 2026