SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Propylthiouracil Tablets 50 mg

2. Qualitative and quantitative composition

Component and quality standard (and grade, if applicable)
Propylthiouracil
Lactose monohydrate spray dried (Flow Lac 100)*
Progelatinised Starch (Lycatab)
Sodium starch glycolate
Maize starch
Purified water
Maize starch
Sodium Starch Glycolate
Magnesium stearate

3. Pharmaceutical form

Solid Dosage Form Tablet

White to off white coloured, round shaped biconvex uncoated tablets plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

Hyperthyroidism

4.2 Posology and method of administration

Adults and elderly:

Initially 300 to 600mg 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 150mg daily and continued for 1-2 years.

In renal *impairment*:	GFR 10 to 50ml/min, 75% dose GFR < 10ml/min, 50% dose
In hepatic disease:	Reduced dose
Children under 6 years:	Not recommended
Children 6-10 years:	Initially 50 to 150mg once daily or in divided doses
Children over 10 years:	Initially 150 to 300mg once daily or in divided doses

4.3 Contraindications

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

Owing to the presence of Lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 Special warnings and precautions for use

Because of 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.

Propylthiouracil may cause hypothrombinaemia and bleeding so prothrombin time should be monitored during therapy, especially prior to surgery.

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 6 months. If significant hepatic enzyme abnormalities develop during treatment with propylthiouracil the drug should be discontinued immediately.

Propylthiouracil should be used with caution in patients with renal impairment or hepatic disease. 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.

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 Pregnancy and lactation

Women of childbearing potential

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

Pregnancy

Hyperthyroidism in pregnant women should be adequately treated to prevent serious maternal and foetal complications.

Propylthiouracil is able to cross the human placenta and in high doses may cause foetal goitre and hypothyroidism.

Animal studies are insufficient with respect to reproductive toxicity. Epidemiological studies provide conflicting results regarding the risk of congenital malformations.

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.

Lactation

Propylthiouracil also transfers to breast milk but this does not preclude breast-feeding. Neonatal development and infant thyroid function should be closely monitored. The lowest effective dose should be used.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Blood and lymphatic system: 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.

Ear and labyrinth disorders: Rarely, hearing impairment may occur with propylthiouracil. The impairment usually becomes less marked after withdrawal of the drug.

Gastrointestinal: Nausea, gastrointestinal disturbances, taste perversion. Rarely vomiting.

General: Fever.

Hepatobiliary: 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.

Immune system: 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).

Musculoskeletal*:* Myopathy, arthralgia,

***Nervous system**:* Headache.

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

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 at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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, pruritus, and pancytopenia.

Treatment

The treatment of propylthiouracil overdose should aim to minimise the amount of drug absorbed into 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

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.

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

5.2 Pharmacokinetic properties

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. Most is excreted as the glucuronic acid conjugate in the urine. Plasma half-life is 1-3 hours, the volume of distribution approximately 30l, with about 80% plasma protein binding.

Propylthiouracil crosses the placenta and is secreted in breast milk reaching about 10% of the serum concentration.

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 (approx 45 years ago) 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 excipient

Lactose Monohydrate Spray-Dried (Flow Lac 100)
Pregelatinised Starch (Lycatab)
Sodium Starch Glycolate
Maize Starch
Magnesium Stearate

6.2 Incompatibilities

None known

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Do not store above 30°C. Protected from light and moisture.

6.5 Nature and contents of container

Blister Pack

The product is available in PVC/Aluminium foil. 10 Tablets are packed in a PVC blister. Such 10 blisters of 10 tablets each are packed in a carton along with insert

HDPE bottle pack

HDPE bottle pack comprises of 30 cc white opaque round HDPE bottle with 28 mm neck and closed with 28 mm opaque polypropylene continuous threaded closure with induction sealing liner. The HDPE bottle is then packed in carton along with the leaflet.

6.6 Special precautions for disposal and other handling

The tablets are administered orally.

7. Marketing authorisation holder
Acme Formulation Pvt. Ltd India
Ropar Road Nalagarh, Distt. Solan, Himachal Pradesh (India) 174101

8. Marketing authorisation number(s)

09397/10291/NMR/2022

9. Date of first authorisation/renewal of the authorization
Dec 31, 2023

10. Date of revision of the text