SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Propylthiouracil 100mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Propylthiouracil 100mg

Excipient with known effect: This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essential 'sodium-free'.

3 PHARMACEUTICAL FORM

White, circular, biconvex uncoated tablets with "F" and "I2" debossed on either side of breakline on one side and plain on other side (Approximate Size: 8 mm)

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1. Management of hyperthyroidism, including the treatment of Graves' disease and thyrotoxicosis.
2. Amelioration of hyperthyroidism in preparation for surgical treatment.
3. An adjunct to radioactive iodine therapy.
4. In juvenile hyperthyroidism to delay ablative therapy.
5. To manage thyrotoxic crisis.

4.2 Posology and method of administration

Propylthiouracil is administered by the oral route.

Adults:

Management of Hyperthyroidism

The initial dose of propylthiouracil is between 300mg and 600mg given as a single daily dose. This dose should be maintained until the patient becomes euthyroid. The dose should then be reduced gradually to a maintenance dose of between 50mg and 150mg, taken as a single daily dose.

Daily doses can be divided if preferred.

Preparation for Surgery

As for management of hyperthyroidism, until the patient becomes euthyroid.

Adjunct to Radioactive Iodine Therapy

As for management of hyperthyroidism, for several weeks prior to radioiodine treatment. Withdraw propylthiouracil 2 to 4 days before irradiation. The dosage of radio-iodine may need to be adjusted because propylthiouracil may have a radioprotective effect.

Management of Thyrotoxic Crisis

200mg every 4 to 6 hours for the first 24 hours, decrease the dose as the crisis subsides.

Elderly

The adult dose should apply, but caution is advised in the presence of renal or hepatic impairment, where a dosage reduction may be justified.

Children:

Juvenile Hyperthyroidism

Children aged 6 - 10 years: Initial dose of 50-150mg daily or in divided doses

Children over 10 years: Initial dose of 150-300mg (or 150mg/m2) daily or in divided doses

Maintenance dose is determined by the patient's response.

Treatment of Hyperthyroidism in Neonates:

5-10mg/kg daily.

No other specific children's doses are known.

4.3 Contraindications

A known hypersensitivity to propylthiouracil.

4.4 Special warnings and precautions for use

Patients should be made aware that the development of certain adverse effects (fever, mouth ulcers, rashes, sore throat) may be an indication of agranulocytosis, a serious reaction to the drug, and they should contact their doctor immediately as treatment should be stopped. A full blood count should be performed if there is clinical evidence of infection. Likewise propylthiouracil should be used with extreme caution in patients receiving other drugs known to cause agranulocytosis. Use propylthiouracil with caution in patients more than 40 years old.

Decrease the dose of propylthiouracil in renal failure. If the glomerular filtration rate is 10-50ml/min, decrease dose by 25%. If the GFR is <10ml/min decrease dose by 50%.

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

Discontinue propylthiouracil if clinically important evidence of abnormal liver function occurs.

Prolonged therapy and/or excessive doses of propylthiouracil may cause hypothyroidism so thyroid function should be monitored regularly.

Another serious side effect is systemic vascultis which can occur anytime and up to several years after initiation of treatment with propylthiouracil. Risk of systemic vasculitis may increase with prolonged use. Renal involvement is most common but skin, lung and musculoskeletal systems may also be involved. In severe cases death can occur. Propylthiouracil should be discontinued promptly and treatment initiated as required.

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 (see 4.8).

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

The response of the thyroid gland to propylthiouracil may be impaired by a concurrent high iodine intake.

Drug induced changes in thyroid status may affect the dosage requirements for theophylline and digitalis. The doses of digitalis and theophylline may need to be reduced as thyroid function returns to normal.

4.6 Fertility, Pregnancy and lactation

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.

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.

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.

A strict 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.

4.7 Effects on ability to drive and use machines

Propylthiouracil has no documented effects on the ability to drive or use machines.

4.8 Undesirable effects

Minor adverse effects of propylthiouracil include: rash, urticaria, pruritus, abnormal hair loss, skin pigmentation, oedema, nausea, vomiting, epigastric distress, loss of taste, arthralgia, myalgia, paresthesia and headache.

Leucopenia is a common adverse effect, but it is usually mild and reversible.

Agranulocytosis is the most serious adverse effect of propylthiouracil, but the incidence is very low. It tends to occur within the first two months of therapy and patients over the age of 40 years and receiving larger doses are at greater risk.

Frequency unknown: Hepatitis, Hepatic Failure

Other severe, but infrequent adverse events include: aplastic anaemia; drug fever; lupus- like syndrome; severe hepatic reactions (including encephalopathy, fulminant hepatic necrosis and death); periarteritis; hypoprothrombinaemia; thrombocytopenia and bleeding.

Nephritis, interstitial pneumonitis, cutaneous and systemic vasculitis and polymyositis have also been reported. Hypersensitivity reactions may be associated with the development of anti-neutrophil cytoplasmic antibodies (ANCA).

Propylthiouracil-induced hepatoxicity is rare and usually manifests as hepatocellular hepatitis with or without jaundice. Cholestatic jaundice has also occurred. Adverse liver effects are generally reversible on cessation of propylthiouracil.

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

4.9 Overdose

Symptoms of propylthiouracil overdose include: nausea, vomiting, epigastric distress, headache, fever, arthralgia, pruritus, oedema and pancytopenia, exfoliative dermatitis and hepatitis have occurred. Agranulocytosis is the most severe potential adverse effect due to acute propylthiouracil toxicity.

The treatment of propylthiouracil overdose should aim to minimise the amount of drug absorbed into the circulation. Following acute toxicity the stomach should be emptied by gastric lavage or emesis. 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 blocks the production of thyroid hormones by inhibiting the enzyme thyroid peroxidase. This prevents the incorporation of iodine into tyrosyl residues of thyroglobulin and inhibits the coupling of the iodotyrosyl residues to form iodothyronine. It also interferes with the oxidation of iodide ion and iodotyrosyl groups.

Propylthiouracil does not inhibit the action or release of already formed thyroid hormone nor does it interfere with the effectiveness of circulating or exogenously

administered thyroid hormone. It does, however, inhibit the peripheral de-iodination of thyroxine to tri-iodothyronine. Propylthiouracil also causes a gradual reduction in the level of circulating thyroid stimulating immunoglobulins in Grave's disease.

5.2 Pharmacokinetic properties

Absorption

Propylthiouracil is rapidly absorbed from the gastro-intestinal tract and has a bioavailability of 50-75%.

Half-Life

The elimination half-life of propylthiouracil is estimated to be 1-2 hours. The elimination half-life may be increased in hepatic and renal impairment and a dosage reduction may be warranted. Despite its short half-life, propylthiouracil is retained in the thyroid gland for at least 24 hours.

Distribution

Propylthiouracil appears to be concentrated in the thyroid gland. It readily crosses the placenta and is distributed into breast milk. About 80% of propylthiouracil is protein bound.

Metabolism

Propylthiouracil undergoes rapid first-pass metabolism in the liver where it is metabolised to its glucuronic acid conjugate.

Excretion

Propylthiouracil is mainly excreted in the urine as the glucuronic acid conjugate. Very little unchanged drug is excreted in the urine and negligible amounts are excreted in the faeces.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose

Pregelatinized Starch

Sodium Starch Glycolate Type A

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years

Shelf life after opening of container: 100 days

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

Blister packs (Alu-Clear PVC blister pack): Blister pack comprises of Clear film PVC 250µ as a forming material and Plain 25µ Aluminium foil/ 6-8 gsm HSL as the lidding material.

Container Pack: Container: Round, white, HW HDPE

Closure: Child resistant with HS 123 white printed liner

Pack size: 28, 30, 56, 60, 84, 90 and 100 Tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Macleods Pharma UK Limited,
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Wynyard, Billingham,
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8 MARKETING AUTHORISATION NUMBER(S)

PL 34771/0257

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08/02/2026