Summary of Product Characteristics

PROPYL-THIOCIL

1. NAME OF THE MEDICINAL PRODUCT

Propyl-Thiocil

Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Propyl-Thiocil tablet contains 50 mg Propylthiouracil.

Excipients with known effect:
Each Tablet contains 22 mg of lactose monohydrate.
Each Tablet contains 0.06 mg of sodium benzoate (E211).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

White, flat beveled tablet, scored in half on one side of the tablet, engraved "TEVA" on the other side of the tablet.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses. The tablet can be crushed.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Propyl-Thiocil is indicated for hyperthyroidism.

4.2. Posology and method of administration

Propylthiouracil is administered by the oral route.

Note: The total daily dosage is usually given in 3 equal doses at approximately 8-hour intervals.
The tablets can be divided. They must not be chewed or crushed.

Adults

Initial Dosage

200-300 mg daily, in divided doses. In patients with severe hyperthyroidism, very large goiters, or both, the initial dosage should usually be 400 mg daily. An occasional patient may require 600-900 mg/day initially.

Maintenance Dosage

100-150 mg daily. This may be increased according to the degree of severity of the individual case.

Children 6-10 Years of Age

Initial Dosage

50-150 mg daily.

Maintenance Dosage

The maintenance dosage should be determined according to the response of the patient.

Children over 10 Years of Age

Initial Dosage

150-300 mg daily.

Maintenance Dosage

The maintenance dosage should be determined according to the response of the patient.

4.3. Contraindications

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

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 medicinal products 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 10-50 ml/min, decrease dose by 25%. If the GFR is <10 ml/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 vasculitis 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 section 4.8).

Excipients:

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

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.
This medicine contains 0.06 mg sodium benzoate (E211) in each tablet. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

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

Pregnancy
Hyperthyroidism in pregnant women should be adequately treated to prevent serious maternal and foetal complications.
Propylthiouracil is able to cross the human placenta.
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 is present in breast milk in small amounts and neonatal development should be closely monitored in any nursing mother treated with this drug.

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

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.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

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 minimize 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

Pharmacotherapeutic group: Antithyroid Preparations, ATC code: H03BA02

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 metabolized 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

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

Starch, lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, gelatin, magnesium stearate, sodium benzoate (E 211).

6.2. Incompatibilities

Not known.

6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4. Special precautions for storage

Store in a dark and dry place below 25°C.

6.5. Nature and contents of container

PVC/aluminum blisters.
Pack sizes: 30 or 90 tablets. Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

No special precautions are required.

7. LICENCE HOLDER AND MANUFACTURER

Teva Pharmaceutical Industries Ltd.
P.O.Box 3190, Petah-Tiqva

8. REGISTRATION NUMBER

026.63.21054

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This leaflet was revised in March 2021 according to MOHs guidelines.