

PRODUCT SHORT INFORMATION

1. NAME OF THE HUMAN MEDICAL PRODUCT

PROPYCİL 50 mg tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:

Each tablet contains:

Propylthiouracil Contains 50 mg

Excipients:

Each tablet contains:

Lactose monohydrate (obtained from bovine milk) 20 mg Powdered sugar 9 mg

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Tablet

White, round tablet with a notch on one side

4. CLINICAL FEATURES

4.1. Therapeutic indications

PROPYCİL,

- Hyperthyroidism
- Basedow-Graves disease
- Making the patient euthyroid before surgery • In case of post-operative recurrences,
- It is used in thyroid crises.

In children, propylthiouracil should be used when methimazole and other alternative treatments are not available.

4.2. Posology and method of administration

Generally, propylthiouracil is taken every 6-8 hours.

Dosage / frequency and duration of application

Use for adults, teenagers and children over 10 years of age:

Recommended starting dose:

For the treatment of moderate hyperthyroidism, 100-300 mg propylthiouracil is initially given daily, which should be taken in 2 or 3 doses, each dose varying between 50-100 mg (1-2 tablets).

The recommended initial daily dose for the treatment of severe hyperthyroidism or iodine contamination varies

between 300 and 600 mg (4-6 times daily) . This document has been signed electronically in accordance with the

Electronic Signature Law No. 5070. Document verification code: 1Z1AxM0FyYnUyak1UYnUyZmxXYnUy
It can be checked at the address. Secure electronic signature is the same as the original. Document verification code: 1Z1AxM0FyYnUyak1UYnUyZmxXYnUy

Treatment of thyrotoxicosis crisis:

To assist in treatment, 200 mg (4 tablets) is taken orally at 4-hour intervals on the first day. The dose is reduced according to the course of the crisis.

Frequency and duration of application:

Once the clinical symptoms disappear, the dose is gradually reduced to the maintenance dose.

When body weight increases beyond normal, the amount of medication is further reduced.

Once the patient is stable (usually 1-2 months after starting treatment), maintenance therapy is started.

The maintenance dose is 50-150 mg and treatment is continued for 1-2 years.

How to apply:

For oral use only.

Tablets are taken whole with a small amount of liquid without chewing. Foods may increase or decrease the absorption of PROPYCIL. It is recommended to take PROPYCIL at a certain time daily.

Additional information regarding special populations:

Kidney failure:

The dose should be reduced by 25% in patients with mild to moderate renal insufficiency (GFR: 10-50 mL/min) and by 50% in patients with severe renal insufficiency (GFR \leq 10 mL/min).

Liver failure:

The dose should be reduced in patients with hepatic insufficiency.

It is recommended to analyze liver and kidney functions before starting PROPYCIL treatment.

Pediatric population:

For children aged 6-10 years, the starting dose is 50 mg once daily or in divided doses.

It is 150 mg.

The safety and effectiveness of the drug in children younger than 6 years of age are not known.

Geriatric population:

The lowest dose is recommended. Since elderly patients are more likely to have decreased renal, hepatic or cardiac function and concomitant diseases, care should be taken in dose selection in the elderly.

4.3. Contraindications

PROPYCIL, •

In patients who are sensitive to propylthiouracil or any of the excipients included in the tablet composition.

- In patients with hypersensitivity to other antithyroid drugs.
- In patients with substernal goiter • If

previous treatment using propylthiouracil has had adverse effects on the patient (especially after severe hepatic lesion caused by agranulocytosis and hepatitis) is contraindicated.

PROPYCIL should be given with caution under the supervision of a physician in patients with abnormal blood cell counts or increased levels of transaminases or enzymes indicating cholestasis.

4.4. Special usage warnings and precautions

Liver toxicity:

Serious hepatic reactions, including fatalities and cases requiring liver transplantation, have been reported in both pediatric and adult patients during propylthiouracil therapy.

The course of recovery varies, with most cases showing hepatic reactions within 6 months. If significant abnormalities in hepatic enzymes occur during propylthiouracil therapy, the drug should be discontinued immediately (see section 4.8).

Patients should be warned to report symptoms of liver dysfunction (anorexia, pruritus, right upper quadrant pain), especially during the first 6 months of treatment. If these symptoms occur, the drug should be discontinued and liver function tests and ALT and AST values should be obtained.

When propylthiouracil is used during pregnancy, or if the patient becomes pregnant while taking propylthiouracil, the patient should be warned about the rare potential for maternal and fetal liver damage (see section 4.6).

Agranulocytosis:

Agranulocytosis is a potentially life-threatening side effect of propylthiouracil therapy and occurs in approximately 0.2% to 0.5% of patients. Agranulocytosis typically occurs within the first 3 months of therapy. Patients should be instructed to promptly report symptoms suggestive of agranulocytosis, such as fever or sore throat.

Agranulocytosis may occur within a few hours. Although the probability of occurrence is low in most cases, the patient should be informed about the clinical signs of agranulocytosis (fever, malaise, tonsillar angina, stomatitis) and the need for urgent blood cell counts. In the presence of neutropenia confirmed by clinical or laboratory findings, treatment should be stopped immediately.

A complete blood count must be performed before starting treatment with PROPYCIL.

This count should also be performed during treatment.

If agranulocytosis is suspected, PROPYCIL should be discontinued immediately. In addition, a granulocyte colony-stimulating factor (G-CSF) should be administered after consultation with a hematologist. implementation may be considered (see Section 4.8).

Leukopenia, thrombocytopenia, and aplastic anemia may also occur. Aplastic anemia, ANCA-positive vasculitis, hepatitis, interstitial pneumonitis, unexplained fever, or

In case of exfoliative dermatitis, PROPYCIL should be discontinued.

Vasculitis:

Serious complications and death have been reported in patients treated with propylthiouracil.

Cases of vasculitis include glomerulonephritis, leukocytoclastic cutaneous vasculitis, alveolar/pulmonary hemorrhage, cerebral angiitis, and ischemic colitis. Many cases have been associated with anti-neutrophil cytoplasmic antibody (ANCA)-positive vasculitis. In some cases, vasculitis has resolved with discontinuation of the drug. However, more severe cases have required therapies such as corticosteroids, immunosuppressants, and plasmapheresis. If vasculitis is suspected in a patient, treatment should be discontinued and appropriate therapy should be initiated.

Patients should be warned about the potential for serious complications and even death with the use of propylthiouracil. Patients should be instructed to promptly report symptoms that may be associated with vasculitis, including rash, hematuria or decreased urine output, dyspnea, or hemoptysis.

Propylthiouracil crosses the placenta. Fetal goiter and cretinism have been reported following maternal administration of propylthiouracil (see section 4.6).

The safety and effectiveness of the drug in children younger than 6 years of age are not known.

Propylthiouracil therapy is recommended in pediatric patients only in cases where methimazole is not tolerated or when radioactive iodine and surgical treatments are not appropriate.

In some patients with goiter, the goiter may enlarge. Propylthiouracil may cause hypothyroidism, which requires routine monitoring of TSH and free T4 levels with dose adjustments to maintain euthyroidism.

In order to control the possibility of hypoprothrombinemia and hemorrhage, prothrombin time determinations should be made, especially before surgery.

Propylthiouracil should be used with caution in patients with liver disease or renal impairment (see section 4.2 Dose and method of administration). Hepatic necrosis development may have fatal consequences (see section 4.8 Undesirable effects).

PROPYCIL; contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not use this medicine.

PROPYCIL; contains powdered sugar Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not use this medicine.

4.5. Interactions with other medical products and other forms of interaction

The use of thyroxine reduces the uptake of propylthiouracil by the thyroid gland, requiring greater suppression of the synthesis of its endogenous hormone. For greater suppression of the thyroid, greater doses of propylthiouracil are required.

The antithyroid effect of PROPYCIL is reduced when used with iodine or in the presence of previous contamination with iodine-containing drugs or X-light contrast. The onset of euthyroidism is delayed.

Pretreatment with propylthiouracil may reduce the effectiveness of radioactive iodine (^{131}I) treatment of hyperthyroidism.

The activity of oral anticoagulants (e.g. warfarin) may be increased due to potential inhibition of vitamin K activity by propylthiouracil. Additional monitoring of PT/INR may be required, especially before surgery.

Hyperthyroidism may increase the clearance of beta-blockers through a high extraction ratio. The dose of beta-adrenergic blockers may need to be reduced after a hyperthyroid patient becomes euthyroid.

In hyperthyroid patients who regularly use digitalis glycosides, serum digitalis levels may increase after they become euthyroid, and therefore the digitalis dose may need to be reduced.

In hyperthyroid patients who use theophylline regularly, theophylline clearance may decrease after they become euthyroid, and theophylline dose may need to be reduced.

Additional information on special populations

Pediatric population:

No specific interactions have been found in the pediatric population.

4.6 Pregnancy and lactation

General advice

Pregnancy Category: D

Women of childbearing potential/Birth control (Contraception)

There is no information regarding its use in women of childbearing potential.

Uncontrolled maternal hyperthyroidism may cause adverse outcomes in the neonate (e.g., premature birth, low birth weight) and the mother (e.g., preeclampsia, congestive heart failure, stillbirth, miscarriage). To prevent fetal and maternal adverse events, normal thyroid function should be maintained before conception and throughout pregnancy.

Pregnancy Period

Pharmacological effects of propylthiouracil on pregnancy and/or fetus

PROPYCIL should not be used during pregnancy unless necessary (to control maternal hyperthyroidism).

Animal studies are inconclusive regarding the reproductive toxicity of propylthiouracil.

Epidemiological studies have yielded conflicting results regarding the risk of congenital malformations. is giving.

Antithyroid therapy may be recommended to control hyperthyroidism during pregnancy. Propylthiouracil is considered first-line therapy, especially in the first trimester and immediately before, because of congenital anomalies observed with methimazole therapy. In the second and third trimesters, methimazole may be preferred because of the risk of liver toxicity (see section 4.4) with propylthiouracil. In later pregnancy, propylthiouracil doses may be reduced and discontinued weeks/months before delivery.

Propylthiouracil crosses the placenta. Adverse reactions including fetal and neonatal hypothyroidism, goitre, cretinism and hyperthyroidism have been reported following maternal administration of propylthiouracil.

When used during pregnancy or when pregnancy occurs while the drug is being used, the patient should be warned about the potential for liver damage in the mother and fetus, which has been observed rarely (see WARNINGS AND PRECAUTIONS). (Section 4.4).

PROPYCIL should be used during pregnancy only at the lowest effective dose, after individual benefit/risk assessment, under doctor's supervision and at an appropriate dose, without adding thyroid hormone drugs. If used during pregnancy, close maternal, fetal and neonatal monitoring is recommended.

Lactation period

Since propylthiouracil is excreted in milk, goiter may occur in breastfed babies of mothers taking the drug. When deciding whether to stop propylthiouracil treatment, the potential benefit to potential risk should be evaluated. If it is decided to be used during lactation, the development of the newborn and the thyroid functions of the baby should be closely monitored.

Reproductive ability / Fertility

There are no studies on its effects on reproductive ability.

4.7. Effects on the ability to drive and use machines

There are no studies on the effect of the drug on the use of vehicles and machines. According to its pharmacological properties, no risk is expected during the performance of such activities. The clinical condition of the patient and possible side effects should be taken into consideration before using vehicles and machines .

This document has been signed electronically in accordance with the Electronic Signature Law No. 5070.

Document <https://www.turkiye.gov.tr/saglik-titck-ebys> must be kept available. It can be checked at the address. Secure electronic signature is the same as the original. Document verification code: 1Z1AxM0FYnUyak1UYnUyZmxXYnUy

4.8. Undesirable effects

Propylthiouracil is generally well tolerated and has low toxicity. Side effects are generally mild and rarely require discontinuation of therapy. In general, antithyroid

Side effects may occur in the first 2 months of treatment with these drugs. As with all thyroid inhibitors, leukopenia or agranulocytosis may occur in some cases. For this reason, PROPYCIL should be used under the supervision of a doctor and blood tests should be performed during the first month of use.

There is a tendency to hemorrhage as a rare complication in treatment with antithyroid drugs. Fitomenadion can be brought under control by giving

Very common (≥1/10), common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from available data)

Blood and lymphatic system diseases:

Common: Neutropenia (not clinically significant)

Uncommon: Agranulocytosis.

Very rare: Thrombocytopenia, pancytopenia, impaired erythropoiesis, hemolysis, positive Coombs test, lymphadenopathy, aplastic anemia, leukopenia, hemorrhage.

Agranulocytosis may occur in 0.3-0.6% of cases. It may also occur weeks/months after initiation of treatment and may lead to permanent discontinuation of the drug.

In most cases, agranulocytosis resolves after discontinuation of the drug. Administration of granulocyte colony-stimulating factor (G-CSF) may be necessary in consultation with a haematologist (see Precautions). (Section 4.4).

Immune system diseases:

Common: Hypersensitivity reactions, usually presenting as allergic skin reactions (pruritus, rash, urticaria). These conditions are not severe and regress with continued treatment (see Skin and subcutaneous tissue disorders).

Rare: Drug fever, liver injury (see Hepatobiliary disorders).

Very rare: Arthralgia (see Musculoskeletal disorders, connective tissue and bone disorders)

Endocrine diseases:

Very rare: Goiter (in newborns)

Unknown: Swelling of the salivary glands

Metabolism and nutritional diseases:

Unknown: Weight gain

Diseases of the nervous system:

Rare: Dizziness, neuromuscular disorder.

Not known: Dizziness, headache, vertigo, paresthesia, fever

Ear and inner ear diseases:

Very rare: Hearing loss, this effect usually subsides after discontinuation of the drug.

This document has been signed electronically in accordance with the Electronic Signature Law No. 5070. Proof of the document can be checked at the address. Secure electronic signature is the same as the original. Document verification code: 1Z1AxM0FyYnUyak1UYnUyZmxXYnUy

Vascular diseases:

Very rare: ANCA positive vasculitis, cutaneous vasculitis, leukocytoclastic vasculitis, lupus-like syndrome, spotty periarteritis, peripheral edema

Respiratory, thoracic and mediastinal disorders:

Very rare: Interstitial pneumonia, asthma.

Unknown: Alveolar hemorrhage

Gastrointestinal diseases:

Common: Gastrointestinal upset, nausea, stomach pain, vomiting

Uncommon: Taste and smell disorders (dysgeusia, ageusia) (reversible, improving within a few weeks after stopping treatment).

Unknown: Constipation

Hepatobiliary diseases:

Rare: Liver damage (in case of high dosage). Reports of reactions including hepatitis, hepatocellular necrosis and transient cholestasis have been reported. Symptoms disappear after discontinuation of the drug. Before initiating treatment with propylthiouracil, it should be remembered that hyperthyroidism itself may cause an increase in gamma glutamyltransferase and alkaline phosphatase levels.

Very rare: Severe hepatic impairment.

Not known: Hepatitis, liver failure

Skin and subcutaneous tissue diseases:

Common: Pruritic rash, urticaria.

Very rare: Alopecia, peripheral edema.

Not known: Erythema nodosum, exfoliative dermatitis, Systemic lupus erythematosus (SLE) Syndrome like

Musculoskeletal disorders, connective tissue and bone diseases:

Very rare: Arthralgia without signs of inflammation

Kidney and urinary tract diseases:

Not known: Acute renal failure, glomerulonephritis, nephritis

Studies:

Very common: Transient increase in transaminases.

Weight gain may occur during propylthiouracil treatment due to the reduction of excessive energy loss caused by hyperthyroidism. Patients should be informed that energy loss will return to normal after resolution of the disease.

Thyroid function should be monitored regularly during thyreostatic therapy.

High dose thyreostatic therapy may cause goiter formation or further growth of existing goiter. This may be seen in intrathoracic goiter, which may extend into the trachea. In addition, there is a risk of clinical and subclinical hypothyroidism as a result of high dose administration. The dose of propylthiouracil should be reduced after euthyroidism is achieved or levothyroxine is administered. When thyroxine therapy is administered, propylthiouracil its use should not be stopped completely.

Goiter formation in cases where TSH is depressed and during propylthiouracil treatment It is a general feature of the disease and cannot be prevented by additional thyroid hormones. The occurrence and progression of endocrine orbitopathy is independent of thyroid diseases. is the situation.

This complication should not be a reason for reconsideration of treatment. (thyreostatic therapy, surgery, radioiodine) and as an undesirable effect of the appropriate treatment method should not be evaluated.

Delayed hypothyroidism may be seen rarely. It is related to the inflammation process of the thyroid tissue.

This should not be considered as a side effect of treatment.

During treatment with propylthiouracil, continuous monitoring of blood cells, transaminases and cholestasis indicator enzymes is recommended.

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions after licensing is of great importance. Reporting allows continuous monitoring of the benefit/risk balance of the drug. Healthcare professionals are required to report any suspected adverse reactions to the Turkish Pharmacovigilance Center (TÜFAM) (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel: 0 800 314 00 08; fax: 0 312 218 35 99).

4.9. Overdose and treatment

Overdose symptoms:

Goiter and hypothyroidism may be induced by repeated overdosage. Nausea, vomiting, epigastric distress, headache, fever, arthralgia, pruritus, edema, pancytopenia, aplastic anemia, central nervous system stimulation or depression are prominent symptoms.

Treatment of overdose:

The drug should be discontinued, and general and supportive treatment should be applied according to the clinical condition of the patient. Treatment may include monitoring of bone marrow response, forced diuresis, peritoneal, hemodialysis, and even charcoal hemoperfusion. A complete blood count should be considered due to the risk of rare hematological complications. If bone marrow depression develops, appropriate treatment should be applied.

There is no specific antidote to propylthiouracil.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic Group: Antithyroid drugs, Thyroid drugs

ATC Code: H03BA02

Propylthiouracil acts in the treatment of hyperthyroidism by inhibiting the synthesis of thyroid hormones, the oxidation of iodine in the thyroid gland, and the synthesis of thyroxine (T4) and triiodothyronine (T3). These properties allow symptomatic treatment of hyperthyroidism, regardless of etiology.

Propylthiouracil does not inactivate thyroxine and triiodothyronine already synthesized in the thyroid gland or in circulation; nor does it interact with exogenously administered thyroid hormones.

Propylthiouracil inhibits the conversion of thyroxine to triiodothyronine in peripheral tissue and thus may be effective in thyroid crises (severe hyperthyroidism).

During the treatment period and within 2-3 weeks, the patient's basal metabolism decreases, he/she begins to gain weight, tachycardia and vasomotor disorders improve, and the pulse rate normalizes. It provides these effects without damaging the thyroid tissue.

5.2. Pharmacokinetic properties

General features

Absorption:

Propylthiouracil is rapidly absorbed from the gastrointestinal tract. After oral administration, maximum plasma concentrations are reached within 1-2 hours. Bioavailability is 80-95%. –

Distribution:

It is 75-80% protein bound. Despite its high protein binding in the blood, its half-life is relatively short. However, the inhibition period in thyroid hormone biosynthesis is much longer. It accumulates in the thyroid gland.

Biotransformation: _____

Propylthiouracil is metabolized in the liver and excreted in the urine. The majority of the dose is eliminated unchanged, with very little as the glucuronic acid conjugate.

Elimination: _____

The elimination half-life of propylthiouracil from plasma is approximately 1-2 hours.

Linearity/Nonlinearity: _____

No information available.

5.3. Preclinical safety data

Acute toxicity

The LD50 of propylthiouracil in male rats is 1.98 g/kg body weight po.

Repeated dose toxicity

Subacute toxicity in rats using different application methods

Studies have identified toxic effects related to dose levels, such as increased body weight, thyroid hyperplasia, leukopenia and hepatomegaly.

Mutagen / Carcinogen

The mutagenic properties of propylthiouracil have not been fully evaluated. Studies on different animals have shown an increase in thyroid tumor rates and hypotrophy after oral administration.

When combined with known carcinogenic substances, greater effects have been observed. There is no scientific study on humans that clearly demonstrates that tumors occur after anti-roid therapy using propylthiouracil.

Reproductive toxicity

In experiments on rats, endocrinological and neurological disorders and excessive pharmacodynamic effects (perinatal hypothyroidism with normochromic anemia) were detected in rat offspring.

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

Povidon K 30

Lactose monohydrate (derived from bovine milk)

Magnesium stearate

Cornstarch

Aerosil 200

Powdered sugar

Ethyl alcohol 96% (removed during drying)

6.2. Incompatibilities

No incompatibilities are known.

6.3. Shelf life

36 is

6.4. Special precautions regarding storage

It should be stored at room temperature below 25°C.

It should be kept in its packaging and out of sight and reach of children.

6.5 Nature and content of packaging

PROPYCIL is available in blister packs of 20 and 50 tablets in a cardboard box.

6.6 Disposal of residual materials from human medicinal products and other special precautions

Unused products or waste materials must be disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging and Packaging Waste Control Regulation".

7. LICENSE HOLDER

Recordati Pharmaceutical Industry
and Trade Inc. Ç.OSB Karaağaç Mah. Atatürk Cad.
No:36 Kapaklı / TEKİRDAĞ
Tel: 0282 999 16 00

8. LICENSE NUMBER

106/13

9. FIRST LICENSE DATE / LICENSE RENEWAL DATE First licensing date:

11.11.1970 License renewal date:

07.10.2015

10. RENEWAL HISTORY OF KUB

--/------