PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]**PROPYLTHIOURACIL TABLETS**

Propylthiouracil
Tablets, 50 mg, Oral
USP

ATC Code: H03BA02
Thyroid therapy

Phebra Canada Inc.
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Montreal, QC
Canada, H4S 1Z9

Website: www.phebra.com/cae

Date of Initial Authorization:
December 2, 2021

Submission Control Number: 251552

RECENT MAJOR LABEL CHANGES

Section	Date
None at time of authorization	

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

PROPYLTHIOURACIL TABLETS (propylthiouracil tablets) is indicated:

- For the medical management of hyperthyroidism.
- In conjunction with radioiodine to hasten recovery while awaiting the effects of radiation.
- For the control of thyrotoxicosis prior to surgery.
- In the management of a thyroid storm in addition to other therapeutic measures.

1.1 Pediatrics

Pediatrics (<18 years): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (>65 years): Information specific to the geriatric population is not available for this drug product.

2 CONTRAINDICATIONS

- PROPYLTHIOURACIL TABLETS is contraindicated in patients who are hypersensitive to this drug, related thioamide derivatives or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING**.
- PROPYLTHIOURACIL TABLETS is contraindicated in breast-feeding women.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- Agranulocytosis is a potentially life-threatening side effect of PROPYLTHIOURACIL TABLETS therapy. See **7 WARNINGS AND PRECAUTIONS**
- Severe liver injury and acute liver failure, in some cases fatal, have been reported in patients treated with PROPYLTHIOURACIL TABLETS. These reports of hepatic reactions include cases requiring liver transplantation in adult and pediatric patients. See **7 WARNINGS AND PRECAUTIONS**

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Treatment with PROPYLTHIOURACIL TABLETS should be individualized, according to the severity of symptoms and signs of hyperthyroidism and response to therapy.
- Usually after one or 2 weeks, but certainly after 3 weeks of therapy, objective signs of clinical improvement should be seen.
- Delayed responses are sometimes noted when the thyroid is unusually large and when iodine in any form has previously been given.
- The course of therapy may last from 6 months to 3 years. Usually within 1 to 2 years, a prolonged remission in 50% of the cases can be expected.
- When remission is observed, PROPYLTHIOURACIL TABLETS should be withdrawn over a period of 1-2 months under close supervision.

4.2 Recommended Dose and Dosage Adjustment

Adults (≥18 years of age): The recommended initial dose is 50-100 mg (1 to 2 tablets of PROPYLTHIOURACIL TABLETS) every 8 hours, with increases as necessary up to a maximum of 500 mg/day. In some cases, initial doses as high as 900 mg/day may be required.

When doses larger than 300 mg/day of PROPYLTHIOURACIL TABLETS are needed, the drug should be administered every 4 to 6 hours.

The patient should be examined regularly by the physician and the dose of PROPYLTHIOURACIL TABLETS adjusted until the patient is euthyroid (usually after 6-8 weeks). At this stage, the dose should be reduced by 1/3 every 4-6 weeks to a maintenance dosage of one tablet of PROPYLTHIOURACIL TABLETS 2 or 3 times daily, administered at regular intervals.

Geriatric (>65 years of age): No data are available to determine whether subjects aged 65 or over respond differently from younger subjects. Dose selection for an elderly patient should be cautious reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Pediatric (<18 years of age): Health Canada has not authorized an indication for pediatric use.

Hepatic impairment: No clinical studies have been performed with PROPYLTHIOURACIL TABLETS in patients with hepatic insufficiency. Since liver toxicity is associated with the use of PROPYLTHIOURACIL TABLETS, caution is warranted in patients with hepatic impairment.

Renal impairment: No clinical studies have been performed with PROPYLTHIOURACIL TABLETS in patients with renal impairment.

The following schedule is recommended by W.M. Bennett et al[1]:

Glomerular Filtration Rate (creatinine clearance)	10-50 mL/min	<10 mL/min
Reduce dose by	25% of the usual maintenance dose	50% of the usual maintenance dose

1. Bennett WM et al. Guidelines for drug therapy in renal failure. Ann Intern Med 1977; 86:754-83.

4.4 Administration

PROPYLTHIOURACIL TABLETS can be taken with or without food. Patients should be instructed to swallow tablets whole and not to chew, split, or crush tablets. Patients should not ingest if tablets are broken, cracked, or otherwise not intact. PROPYLTHIOURACIL TABLETS should be taken at the same time each day.

4.5 Missed Dose

Advise patients to not double a dose to make up for a missed dose.

Twice-daily dose: If it is less than 6 hours before the patient's next dose, skip the dose they missed and take their next dose when they are meant to. If the patient remembers with 6 or more hours before the next dose, they should take the missed dose as soon as they remember, then take the next dose at the scheduled time.

QID (4 times a day) dose: If it is less than 3 hours before the patient's next dose, skip the dose they missed and take their next dose when they are meant to. If the patient remembers to take PROPYLTHIOURACIL TABLETS with 3 or more hours before the next dose, they should take the missed dose as soon as they remember, then take the next dose at the scheduled time.

5 OVERDOSAGE

Agranulocytosis is the most serious adverse effect resulting from overdose and/or prolonged administration.

There has been one reported case of overdose with PROPYLTHIOURACIL TABLETS in the literature where the patient developed Henoch-Schonlein purpura (HSP) for which causal relationship with the drug could not be confirmed.

Overdosage can result in enlargement of the thyroid gland, with signs and symptoms of hypothyroidism. This can be readily reversed by reducing or even temporarily withdrawing medication. Thyroxine replacement therapy, until the patient becomes euthyroid, may be indicated.

Overdosage in pregnant women may result in congenital goiter and hypothyroidism in the fetus. The newborn child should be examined carefully for signs of hypothyroidism and immediate thyroid therapy should be instituted if hypothyroidism is confirmed.

Haemorrhage may be controlled by the administration of vitamin K1 and the dosage of PROPYLTHIOURACIL TABLETS should be reduced.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1– Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form/Strength/Composition	Non-medicinal Ingredients
Oral	Tablet 50 mg of propylthiouracil	Lactose monohydrate, magnesium stearate, maize starch, povidone and sodium lauryl sulfate

Description

Propylthiouracil is a thioamide derivative which occurs as a white crystalline powder, odourless with a bitter taste, very slightly soluble in water, sparingly soluble in ethanol and soluble in solutions of alkali hydroxides or ammonia.

50 mg tablets: white, round, biconvex and uncoated; one side is debossed 'PRESTAB' and other side is plain.

PROPYLTHIOURACIL TABLETS are supplied in bottles containing 100 tablets.

7 WARNINGS AND PRECAUTIONS

Please see **3 SERIOUS WARNINGS AND PRECAUTIONS BOX**

7.1 Warnings and Precautions Synopsis

PROPYLTHIOURACIL TABLETS should be reserved for patients who cannot tolerate methimazole and in whom radioactive iodine therapy or surgery are not appropriate treatments for the management of hyperthyroidism.

The vascularity and size of the thyroid gland may increase during treatment with PROPYLTHIOURACIL TABLETS. This suggests over treatment and indicates the need for reduced dosage.

Cardiovascular

Vasculitis: Cases of vasculitis resulting in severe complications and death have been reported rarely in patients receiving therapy with PROPYLTHIOURACIL TABLETS.

The cases of vasculitis include: glomerulonephritis, leukocytoclastic cutaneous vasculitis, alveolar/pulmonary hemorrhage, cerebral angiitis, and ischemic colitis. Most cases were associated with anti-neutrophilic cytoplasmic antibodies (ANCA)-positive vasculitis. Early recognition of vasculitis is important to prevent long term organ damage and/or death. Inform patients to promptly report symptoms that may be associated with vasculitis including new rash, hematuria or decreased urine output, dyspnea or hemoptysis.

If vasculitis is suspected, discontinue PROPYLTHIOURACIL TABLETS therapy and initiate appropriate intervention.

Endocrine and Metabolism

Hypothyroidism: Propylthiouracil can cause hypothyroidism necessitating routine monitoring of serum thyrotropin (TSH) and free T4 levels with adjustments in dosing to maintain a euthyroid state. The dose

of PROPYLTHIOURACIL TABLETS should be reduced or temporarily discontinued if signs of hypothyroidism occur during treatment.

Lactose: PROPYLTHIOURACIL TABLETS contains lactose monohydrate. Patients with hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this product.

Hematologic

Agranulocytosis: Agranulocytosis occurs in approximately 0.2% to 0.5% of patients and is a potentially life-threatening side effect of propylthiouracil therapy. Agranulocytosis typically occurs within the first 3 months of therapy. Patients should be instructed to immediately report to their physicians any symptoms suggestive of agranulocytosis, such as sore throat, fever, mouth ulcers, bruising, malaise, non-specific illness or other symptoms of infection. Leukopenia, thrombocytopenia, and aplastic anemia (pancytopenia) may also occur. PROPYLTHIOURACIL TABLETS should be discontinued if agranulocytosis, aplastic anemia (pancytopenia) is suspected, and the patient's bone marrow function should be monitored. A full blood count should be performed and treatment should be discontinued immediately if there is clinical or laboratory evidence of neutropenia. Particular care should be exercised with patients who are receiving concomitant drugs known to be associated with agranulocytosis.

Anticoagulant therapy: Propylthiouracil has occasionally been reported to cause hypoprothrombinemia which would increase the effect of anticoagulants. Doses of oral anticoagulants, administered concurrently, should be adjusted accordingly. See **9.4 Drug-Drug Interactions**

Hepatic/Biliary/Pancreatic

Liver injury resulting in liver failure, liver transplantation, or death, has been reported with propylthiouracil therapy in adult and pediatric patients. Propylthiouracil-induced hepatotoxicity is not dose-related and is thought to be idiosyncratic with an autoimmune component.

Hepatocellular necrosis and fulminant hepatic failure have been reported in patients treated with propylthiouracil. Typically these reactions occur within the first two months of propylthiouracil treatment. Injury is reversible upon discontinuation of propylthiouracil although encephalopathy and/or substantial hepatic necrosis have been reported. Routine monitoring of serum transaminases is not required but may be recommended for patients with a history of liver disease or for those who have other risk factors for hepatitis, e.g. alcohol use.

Discontinue PROPYLTHIOURACIL TABLETS when signs and symptoms of hepatic injury are present (anorexia, pruritus, jaundice, light colored stools, dark urine, right upper quadrant pain, etc.). When these symptoms occur, measurement should be made of liver function (bilirubin, alkaline phosphatase) and hepatocellular integrity (ALT/AST levels). Further thionamide therapy is contraindicated as death has resulted upon rechallenge.

Monitoring and Laboratory Tests

The patient's liver function, hepatic transaminase levels, and the complete blood count should be closely monitored. Blood formula should be determined prior to institution of treatment. Liver Function Tests are also recommended at periodic intervals during therapy. Serum Alkaline Phosphatase, Serum Glutamic Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) levels may be increased.

Thyroid function tests should be monitored periodically during therapy (recommended prior to initiation of therapy, at monthly intervals during stabilization, then every 2 to 3 months) via Free (unbound) Serum Thyroxine (T4) levels, Total Serum T4 levels, Serum Thyrotropin (TSH), Total Serum

Triiodothyronine (T3). Once clinical evidence of hyperthyroidism has resolved, the finding of an elevated serum TSH indicates that a lower maintenance dose of PROPYLTHIOURACIL TABLETS should be employed.

Monitoring of prothrombin time should be considered during therapy with the drug, especially before surgical procedures because PROPYLTHIOURACIL TABLETS may cause hypoprothrombinemia and bleeding. See **8 ADVERSE REACTIONS**

Peri-Operative Considerations

When PROPYLTHIOURACIL TABLETS is administered pre-operatively, iodine, in the form of a strong iodine solution (Lugol's solution or potassium iodide solution) should be given concomitantly for 7-10 days prior to surgery. The rationale for this is to reduce the vascularity and fragility of the thyroid gland.

Renal

PROPYLTHIOURACIL TABLETS should be used with caution in patients with renal impairment.

Respiratory

In view of the fact that hypothyroid patients seem to have poor adrenergic nervous function, PROPYLTHIOURACIL TABLETS should be used with caution in patients with asthma.

Skin

PROPYLTHIOURACIL TABLETS should be discontinued **immediately** at the appearance of a skin rash, as the rash may be, in some instances, followed by dermatological reactions/hypersensitivity syndrome (including Stevens Johnson Syndrome or, toxic epidermal necrolysis). See **8 ADVERSE REACTIONS**

7.2 Special Populations

7.2.1 Pregnant Women

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

Individual benefit/risk assessment is necessary before treatment with PROPYLTHIOURACIL TABLETS during pregnancy. If PROPYLTHIOURACIL TABLETS is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be warned of the potential hazard of the rare potential hazard to the mother and fetus of liver damage.

PROPYLTHIOURACIL TABLETS is suggested for use prior to conception and in the first trimester of pregnancy where clinically appropriate due to the higher risk of congenital abnormalities with methimazole during fetal organogenesis in the first trimester. After the first trimester of pregnancy, the use of an alternative antithyroid medication may be advisable given the potential for maternal hepatotoxicity from PROPYLTHIOURACIL TABLETS.

PROPYLTHIOURACIL TABLETS should be administered during pregnancy at the lowest effective dose, without additional administration of thyroid hormones. Close maternal, fetal and neonatal monitoring of thyroid function is recommended, with adjustment of PROPYLTHIOURACIL TABLETS as necessary.

PROPYLTHIOURACIL TABLETS, used judiciously, is an effective drug for the treatment of hyperthyroidism in pregnant women. However, the drug readily crosses the placental barrier where it can induce goiter and hypothyroidism in the developing fetus. Rare cases of congenital anomalies have been observed post-marketing. See **8.5 Post-Market Adverse Reactions**

Epidemiological studies provide conflicting results regarding the risk of congenital malformations.

7.2.2 Breast-feeding

Propylthiouracil is excreted in breast milk and is contraindicated in nursing mothers. See **2 CONTRAINDICATIONS**

7.2.3 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.2.4 Geriatrics

Geriatrics (>65 years of age): Clinical studies of propylthiouracil did not include sufficient numbers of subjects aged 65 or over to determine whether they respond differently from younger subjects.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most serious adverse reactions associated with PROPYLTHIOURACIL TABLETS are agranulocytosis, hepatotoxicity and rarely, systemic vasculitis. Recovery is often possible following immediate cessation of the drug.

Inhibition of hemopoiesis (agranulocytosis, granulocytopenia, leucopenia, thrombocytopenia) is the most serious side effect. The incidence of agranulocytosis is less than 0.5%. It usually develops in the first few months of therapy, is dose-related and is reversible on rapid withdrawal of the drug.

Leukopenia with granulocytopenia, hemolytic anemia, thrombocytopenia, hypoprothrombinemia with hemorrhagic manifestations, aplastic anemia, myeloblastic leukemia and hyperglobulinemia have been reported.

Severe adverse reactions include liver injury presenting as hepatitis, liver failure necessitating liver transplantation or resulting in death. See **7 WARNINGS AND PRECAUTIONS**

Hepatocellular necrosis and fulminant hepatic failure have been reported in patients treated with PROPYLTHIOURACIL TABLETS. Typically these reactions occur within the first two months of PROPYLTHIOURACIL TABLETS treatment. Injury is reversible upon discontinuation of PROPYLTHIOURACIL TABLETS although encephalopathy and/or substantial hepatic necrosis have been reported. See **7 WARNINGS AND PRECAUTIONS**

Hepatotoxicity has an estimated frequency of 0.1-0.2% in patients treated with PROPYLTHIOURACIL TABLETS. Propylthiouracil-induced hepatotoxicity is not dose-related and is thought to be idiosyncratic with an autoimmune component.

There are reports of a vasculitis associated with the presence of anti-neutrophilic cytoplasmic antibodies (ANCA), resulting in severe complications and death. See **7 WARNINGS AND PRECAUTIONS**

There have been rare reports of serious hypersensitivity reactions (e.g., Stevens Johnson syndrome and toxic epidermal necrolysis) in patients treated with PROPYLTHIOURACIL TABLETS. See **7 WARNINGS AND PRECAUTIONS**

Itching, urticaria, pruritus and a mild papular rash which may be accompanied by purpura are the most common skin reactions; (incidence approximately 3%). Loss or depigmentation of the hair are less frequent. Two cases of vesicular eruption in the newborn have been reported, secondary to maternal PROPYLTHIOURACIL TABLETS therapy.

Other adverse reactions include nausea, vomiting, ageusia, abdominal discomfort, drowsiness, headache, dizziness, arthralgia and paresthesia occur occasionally. Drug fever, lymphadenopathy, splenomegaly, hepatitis, cholestatic jaundice, neuritis, nephritis, unusual increase or decrease in urination, backache, sialadenopathy, recurrent keratitis, conjunctival disorders, connective tissue disorders resembling polyarteritis, arthritis, lupus erythematosus and an ototoxic reaction presenting as unilateral sensorineural hearing impairment.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data Clinical Trial Findings

It should be noted that about 10% of patients with untreated hyperthyroidism have leucopenia (white blood cell count of less than 4,000/mm^3), often with relative granulocytopenia.

8.5 Post-Market Adverse Reactions

Cases of congenital anomalies have been rarely reported in neonates whose mothers were treated with PROPYLTHIOURACIL TABLETS and other drugs during pregnancy. The pattern of congenital anomalies associated with PROPYLTHIOURACIL TABLETS is unclear, but may include anal atresia, accessory auricle, intestinal malrotation, gastrointestinal malformation and ventricular septal defect. See **7.2.1 Pregnant Women**

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Serious Drug Interactions

- Because PROPYLTHIOURACIL TABLETS can cause hypoprothrombinemia, extreme caution is advised in patients receiving oral anticoagulants or heparin. Prothrombin times should be carefully monitored during therapy. See **9.4 Drug-Drug Interactions**
- Concurrent use of PROPYLTHIOURACIL TABLETS with agranulocytosis producing medication may increase the risk of agranulocytosis.

9.2 Drug Interactions Overview

Pre-treatment with PROPYLTHIOURACIL TABLETS may reduce the effectiveness of radio-iodine (^{131}I) therapy for hyperthyroidism.

9.4 Drug-Drug Interactions

Anticoagulants (oral): Due to the potential inhibition of vitamin K activity by propylthiouracil, the activity of oral anticoagulants (e.g. warfarin) may be increased; additional monitoring of PT/INR should be considered, especially before surgical procedures.

Beta-adrenergic blocking agents: Hyperthyroidism may cause an increased clearance of beta blockers with a high extraction ratio. A reduced dose of beta-adrenergic blockers may be needed when a hyperthyroid patient becomes euthyroid.

Digitalis glycosides: Serum digitalis levels may be increased when hyperthyroid patients on a stable digitalis glycoside regimen become euthyroid; a reduced dose of digitalis glycosides may be needed.

Theophylline: Theophylline clearance may decrease when hyperthyroid patients on a stable theophylline regimen become euthyroid; a reduced dose of theophylline may be needed.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Propylthiouracil affects the synthesis of thyroid hormones by inhibiting the incorporation of iodide into thyroglobulin. This is probably done by interfering with the mechanism of oxidation of the iodide ion through thyroid peroxidase activities. It does not inactivate thyroid hormones previously formed or interfere with their release from the gland. The observation that ^{131}iodine uptake remains elevated in hyperthyroid patients even when the euthyroid state is approached suggests that its action may be more complex, involving effects on organic binding and coupling.

Propylthiouracil may also decrease the rate of conversion of T4(1-thyroxine) to T3(triiodothyronine) in peripheral tissues. Iodide uptake is not decreased by propylthiouracil.

Depending on the activity of the disease and on whether or not the patient has previously received iodide, the clinical effects will not appear until the stored supply of thyroid hormones has been utilized. Clinical response may be delayed for up to two weeks.

In responsive patients, prolonged remission may be obtained only after several months of treatment and may take up to several years. The average duration of treatment is usually one year.

Data suggest that stopping therapy as soon as the euthyroid state is attained is as effective in some patients as continuing therapy for a year or longer.

10.2 Pharmacodynamics

The rapidity of the therapeutic response will depend largely on the completeness of blockade of thyroid hormones synthesis, the amount of stored hormones and the peripheral rate of turnover of these hormones.

The effect of a dose of 100 mg of propylthiouracil begins to wear off in 2 to 3 hours; a dose of 500 mg completely inhibits thyroid function for 6 to 8 hours.

10.3 Pharmacokinetics

Absorption: Absorption of effective amounts occurs within 20 to 30 minutes after oral administration.

Distribution: Propylthiouracil labelled with ^{35}S has been found to accumulate in the thyroid gland. Protein binding is about 40%. It crosses the placental barrier and is found in the milk of nursing mothers. The serum or plasma half-life ranges between 1-1.6 hours after a single oral dose.

Metabolism: The metabolites of propylthiouracil have not yet been satisfactorily identified.

Elimination: Propylthiouracil, to the extent of 50% of the dose, is conjugated to glucuronic acid and is mainly excreted via the kidneys within 24 hours. Only a small amount (1-3%) of the drug is found free in the urine.

11 STORAGE, STABILITY AND DISPOSAL

Store at room temperature (15°C to 30°C). Keep this medicine out of the sight and reach of children.

12 SPECIAL HANDLING INSTRUCTIONS

None required.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Propylthiouracil

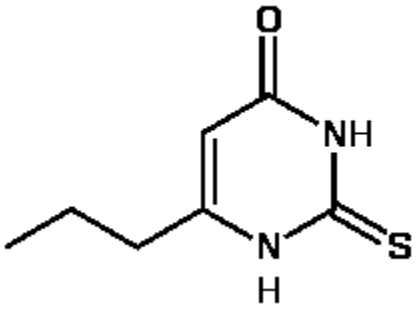
Chemical name: 2,3-Dihydro-6-propyl-2-thioxo-4(1H)-pyrimidinone;
4-hydroxy-2-mercapto-6-propylpyrimidine;
6-n-propyl-2-thiouracil;
6-propyl-2-thiopyrimidine-2,4(1H,3H)-dione;
6-propylthiouracil;
2-mercapto-6-propylpyrimid-4-one;
6-Propyl-2-thiouracil.

Molecular formula and molecular mass:

$C_7H_{10}N_2OS$

170.23 g/mol

Structural formula:



Physicochemical properties:

Description: White or almost white, crystalline powder or crystals.

Melting range: 217 – 221 °C

Solubility: Very slightly soluble in water, sparingly soluble in alcohol. Easily soluble in aqueous ammonia solution and solutions of alkali hydroxides. Practically insoluble in ether, chloroform, benzene.

14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

15 MICROBIOLOGY

No data available.

16 NON-CLINICAL TOXICOLOGY

No data available.

17 SUPPORTING PRODUCT MONOGRAPHS

1. PROPYL-THYRACIL® (50 mg tablets), Control No.: 233767, Prescribing Information, Paladin Labs Inc. (Apr. 06, 2020)
2. PTU™ (50 mg tablets), N/A, Australian Product Information, Phebra Pty Ltd (Feb. 24, 2020)

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrPROPYLTHIOURACIL TABLETS

Read this carefully before you start taking **PROPYLTHIOURACIL TABLETS** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **PROPYLTHIOURACIL TABLETS**.

Serious Warnings and Precautions

- **Agranulocytosis (low white blood cells):** Treatment with PROPYLTHIOURACIL TABLETS can cause agranulocytosis, especially during the initial three months of treatment. This can lead to serious complications or even death. The symptoms can include unusual bleeding, fever, sore throat, bruising, or skin rashes. Your healthcare professional will monitor your health throughout your treatment. However, if you notice any of these symptoms tell your healthcare professional right away. They will stop your treatment if agranulocytosis is suspected.
- **Liver problems:** Treatment with PROPYLTHIOURACIL TABLETS can cause liver injury leading to liver problems, liver failure, or death. This usually occurs during the initial two months of treatment. The symptoms can include: anorexia, itchiness, yellowing of the eyes or skin, light coloured stools, dark urine, and abdominal pain. If these occur your healthcare professional will assess your liver and may decide to stop your treatment.

What is PROPYLTHIOURACIL TABLETS used for?

PROPYLTHIOURACIL TABLETS is used in adults:

- to treat hyperthyroidism (overactive thyroid gland);
- to speed up recovery when used in combination with radioactive iodine therapy;
- to control symptoms of hyperthyroidism before a surgery; and
- to manage symptoms of a thyroid storm (thyroid gland produces too much thyroid hormone in a short period of time).

How does PROPYLTHIOURACIL TABLETS work?

PROPYLTHIOURACIL TABLETS belongs to a group of medications called antithyroid medicines. It works by stopping the thyroid gland from making thyroid hormones. This medication may take a few weeks to reduce the symptoms of hyperthyroidism.

What are the ingredients in PROPYLTHIOURACIL TABLETS?

Medicinal ingredient: propylthiouracil.

Non-medicinal ingredients: lactose monohydrate, magnesium stearate, maize starch, povidone and sodium lauryl sulfate.

PROPYLTHIOURACIL TABLETS comes in the following dosage forms:

Tablets: 50 mg of propylthiouracil.

Do not use PROPYLTHIOURACIL TABLETS if:

- you are allergic to propylthiouracil or any of the other ingredients in PROPYLTHIOURACIL TABLETS;
- you are allergic to similar antithyroid medications known as thioamide derivatives. Ask your healthcare professional if you are unsure;
- you are breastfeeding or planning to breastfeed.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take PROPYLTHIOURACIL TABLETS. Talk about any health conditions or problems you may have, including if you:

- have a low white blood cell count;
- have joint pain;
- have asthma;
- have skin problems;
- have or have had liver problems;
- are taking medications known to be associated with agranulocytosis (ask your healthcare professional if you are unsure);
- have inflamed blood vessels (vasculitis);
- have or have had kidney problems;
- are intolerant to some sugars (e.g., lactose, a milk sugar which is a component of PROPYLTHIOURACIL TABLETS);
- are taking anticoagulant (medications used to prevent your blood from clotting);
- are planning to have a surgery;
- are pregnant, think you may be pregnant, or plan to become pregnant.

Other warnings you should know about:

- **Vasculitis (inflammation of the blood vessel):** Treatment with PROPYLTHIOURACIL TABLETS can cause vasculitis, which can lead to severe organ damage or death. This can occur to the blood vessels in your kidneys, skin, lungs, brain, and intestine. The symptoms of vasculitis include blood in your urine, less urine, a new rash, shortness of breath, or coughing up blood. If you notice any of these symptoms tell your healthcare professional. They may discontinue your treatment and may initiate the appropriate intervention.
- **Hypothyroidism (thyroid gland is producing not enough thyroid hormone):** Treatment with PROPYLTHIOURACIL TABLETS can cause hypothyroidism. The symptoms can include weight gain, tiredness, hair loss, muscle weakness, feeling cold, dry skin, constipation, puffy face, heavier than normal or irregular menstrual periods, and enlarged thyroid gland. If signs of hypothyroidism occur, tell your healthcare professional. They may reduce or temporarily stop your treatment, and may also perform tests to measure your hormone levels.

- **Skin rashes:** Treatment with PROPYLTHIOURACIL TABLETS can cause skin rashes. This can be a sign of an allergic reaction or a skin reaction (e.g., Stevens-Johnson syndrome or toxic epidermal necrolysis). If you notice a skin rash stop taking PROPYLTHIOURACIL TABLETS right away and tell your healthcare professional.
- **Blood problems:** Treatment with PROPYLTHIOURACIL TABLETS can cause decreased levels of red blood cells, white blood cells, and/or blood platelets. Your healthcare professional may do blood tests to monitor the profile of your blood. They may decide to reduce or stop your dose of PROPYLTHIOURACIL TABLETS.

See the **Serious side effects and what to do about them table**, below, for more information on these and other serious side effects.

Monitoring and Testing:

Your healthcare professional will monitor your health which can include doing blood tests. These tests may be performed before and periodically during your treatment to assess the functions of your liver, thyroid, blood, and blood clotting. This will tell your healthcare professional how PROPYLTHIOURACIL TABLETS is affecting you.

Pregnancy:

- If you are pregnant or are able to become pregnant, there are specific risks for you and your unborn baby that you must discuss with your healthcare professional.
- If you are prescribed PROPYLTHIOURACIL TABLETS while you are pregnant, your healthcare professional will also closely monitor you and your unborn baby to ensure that PROPYLTHIOURACIL TABLETS is working correctly. They may also switch your treatment after the first trimester of your pregnancy.
- You should use effective birth control while taking PROPYLTHIOURACIL TABLETS to avoid potential risks.
- If you become pregnant or think you are pregnant while taking PROPYLTHIOURACIL TABLETS, tell your healthcare professional right away.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with PROPYLTHIOURACIL TABLETS:

- medicines that might need a reduced dose when hyperthyroid patients become euthyroid such as:
    - theophylline, a drug used to treat asthma;
    - digoxin, used to treat problems with the rhythm of your heart;
    - beta blockers, used to treat high blood pressure.

You should not take PROPYLTHIOURACIL TABLETS before you have radio-iodine (^{131}I) therapy for an overactive thyroid gland (hyperthyroidism) because it can reduce the effectiveness of radio-iodine (^{131}I) therapy.

Serious Drug Interactions

- Taking PROPYLTHIOURACIL TABLETS with anticoagulants (medicines used to prevent blood clots or thin the blood such as warfarin or heparin), can increase your risk of hypoprothrombinemia (low prothrombin, a blood clotting substance). Ask your healthcare professional if you are unsure.
- Taking PROPYLTHIOURACIL TABLETS with any medications that may lead to agranulocytosis (low white blood cells) may increase your risk of agranulocytosis. Ask your healthcare professional if you are unsure.

How to take PROPYLTHIOURACIL TABLETS:

- You can take PROPYLTHIOURACIL TABLETS with or without food.
- Swallow the tablets whole with a drink of water. Do not chew, split or crush tablets. If the tablet is broken, cracked, or otherwise not intact, do not take the tablet.

Usual dose:

Your healthcare professional will tell you how many tablets to take, and when to take them each day. This will depend on your condition, what other medicines you are taking, and how you respond to treatment with PROPYLTHIOURACIL TABLETS.

When your condition has improved your healthcare professional may put you on a lower dose to maintain your condition.

Overdose:

You may need urgent medical attention in the case of an overdose. An overdose can lead to the following:

- agranulocytosis (low white blood cells);
- hypothyroidism (thyroid gland is producing not enough thyroid hormone);
- haemorrhage (blood loss);
- Henoch-Schonlein purpura (HSP; inflammation of the small blood vessels).

If you think you, or a person you are caring for, have taken too much PROPYLTHIOURACIL TABLETS, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

The actions for a missed dose differ depending on how many tablets you are prescribed to take each day:

- **Two times a day:** If it is less than 6 hours before your next dose, skip the dose you missed, and take the next dose at the scheduled time. If it is more than 6 hours before you next dose, take the missed dose as soon as you remember, and then go back to taking your medicine as you would normally.
- **Four times a day:** If it is less than 3 hours before your next dose, skip the dose and take the next dose at the scheduled time. If it is more than 3 hours before you next dose, take the missed dose as soon as you remember, and then go back to taking your medicine as you would normally.

In both cases, do not try to make up for a missed dose by taking a double dose. This may increase the chances of you getting an unwanted side effect. If you are not sure what to do, ask your healthcare professional.

What are possible side effects from using PROPYLTHIOURACIL TABLETS?

These are not all the possible side effects you may have when taking PROPYLTHIOURACIL TABLETS. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- abdominal discomfort;
- back pain;
- drowsiness;
- burning or prickling sensation in the hands, arms, legs, or feet;
- loss of taste;
- hair loss;
- change in hair colour.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNCOMMON			
Liver problems (including inflammation or damage to the liver, and the death of liver cells)**:** yellowing of the skin or eyes (jaundice), stomach pain or swelling, nausea, vomiting, unusual dark urine, unusual tiredness, fever, light-coloured stool, urine turns dark, and loss of appetite for several days or longer			√
Kidney problems (including kidney inflammation (nephritis))**:** blood in the urine, bruises and blood spots, breathlessness, coughing, swelling of your lymph glands (glands situated around the body which			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
protect against the spread of infection), swelling of the blood vessels in your skin, pain in your lower back / less oxygen to the body, development of anemia			
Agranulocytosis (low white blood cells): unusual bleeding, infections, fever, chills, sore throat, bruising, and skin rashes			√
RARE			
Aplastic anemia (when cells meant to develop into mature blood cells are damaged): fatigue, weakness, and pale skin			√
VERY RARE			
Vasculitis (inflammation of the blood vessels): blood in your urine, less urine, a new rash, shortness of breath, coughing up blood, fever, fatigue, weight loss, and general aches or pains			√
Leukopenia (low white blood cells): infections, fatigue, fever, aches, pains, and flu-like symptoms			√
Thrombocytopenia (low blood platelets): bruising or bleeding for longer than usual if you hurt yourself, fatigue, and weakness			√
Hypothyroidism (thyroid gland is producing not enough thyroid hormone): tiredness, lethargy, muscle weakness, cramps, feeling cold, a slow heart rate, dry, puffy, flaky skin, hair loss, a deep and husky voice, unusual weight gain, change in menstrual periods, listlessness, constipation, headache, and puffy face			√
Allergic reactions (including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)): fever, skin rash, hives, itching, swelling, shortness of breath, wheezing, runny nose, itchy, watery eyes, redness, blistering and/or peeling of the skin and/or inside of the lips, eyes, mouth, nasal passages or genitals, chills, headache, cough, body aches or swollen glands, and redness			√
Encephalopathy (a disease that affects the function or structure of the brain): loss of memory, cognitive impairment, personality changes, inability to concentrate, laziness, coordination or balance problems, muscle twitches, sleep problems, and slurred speech			√

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Anemia (low red blood cells)**:** fatigue, loss of energy, irregular heartbeats, pale complexion, shortness of breath, and weakness			√
Hemolytic anemia (breakdown of red blood cells)**:** pale skin, feeling tired or weak, dizziness, fainting, thirst, and rapid breathing			√
Hypoprothrombinemia (low prothrombin, a blood clotting substance)**:** bleeding or bruising easily, blood in stool, blood in urine, gums bleed easily, nosebleeds, and swelling or pain your joints			√
Myeloblastic leukemia (a type of cancer of the blood and bone marrow)**:** pale skin, tiredness, breathlessness, high body temperature, feeling hot, sweating, weight loss, unusual bleeding, bruising easily, red or purple spots on the skin, bone or joint pain, stomach discomfort, and swollen glands in your neck, armpit or groin			√
Hyperglobulinemia (high globulins in the blood)**:** fatigue, weakness, dizziness, confusion, muscle numbness, tingling, loss of appetite, weight loss, fever, abnormal bleeding, and headaches			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store PROPYLTHIOURACIL TABLETS at room temperature (15°C to 30°C).

Keep out of reach and sight of children.

If you want more information about PROPYLTHIOURACIL TABLETS:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.phebra.com/cae, or by calling 1-866-333-5458.

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