PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr HALYCIL™

Propylthiouracil

Tablets, 50 mg, Oral

BP

ATC Code: H03BA02

Thyroid therapy

Halewood Chemicals Ltd.
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RECENT MAJOR LABEL CHANGES

N/A

TABLE OF CONTENTS

RECENT MAJOR LABEL CHANGES 2
TABLE OF CONTENTS 2
PART I: HEALTH PROFESSIONAL INFORMATION 4
1 INDICATIONS 4
1.1 Pediatrics 4
1.2 Geriatrics 4
2 CONTRAINDICATIONS 4
3 SERIOUS WARNINGS AND PRECAUTIONS BOX 4
4 DOSAGE AND ADMINISTRATION 5
4.1 Dosing Considerations 5
4.2 Recommended Dose and Dosage Adjustment 5
4.4 Administration 6
4.5 Missed Dose 6
5 OVERDOSAGE 6
6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING 6
7 WARNINGS AND PRECAUTIONS 7
7.1 Special Populations 9
7.1.1 Pregnant Women 9
7.1.2 Breast-feeding 10
7.1.3 Pediatrics 10
7.1.4 Geriatrics 10
8 ADVERSE REACTIONS 10
8.1 Adverse Reaction Overview 10
8.5 Post-Market Adverse Reactions 11
9 DRUG INTERACTIONS 11
9.1 Serious Drug Interactions 11
9.2 Drug Interactions Overview 11
9.4 Drug-Drug Interactions 11
9.5 Drug-Food Interactions 12
9.6 Drug-Herb Interactions 12

9.7 Drug-Laboratory Test Interactions....12
10 CLINICAL PHARMACOLOGY....12
10.1 Mechanism of Action....12
10.2 Pharmacodynamics....12
10.3 Pharmacokinetics....12
11 STORAGE, STABILITY AND DISPOSAL....13
12 SPECIAL HANDLING INSTRUCTIONS....13
PART II: SCIENTIFIC INFORMATION....14
13 PHARMACEUTICAL INFORMATION....14
14 CLINICAL TRIALS....14
15 MICROBIOLOGY....14
16 NON-CLINICAL TOXICOLOGY....15
17 SUPPORTING PRODUCT MONOGRAPHS....15
PATIENT MEDICATION INFORMATION....16

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

HALYCIL™ (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): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with no differences in safety or effectiveness.

2 CONTRAINDICATIONS

- HALYCIL 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**.
- HALYCIL 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 HALYCIL 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. 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 HALYCIL 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, HALYCIL 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 HALYCIL) 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 HALYCIL 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 HALYCIL 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 HALYCIL 2 or 3 times daily, administered at regular intervals.

Geriatric (>65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with no differences in safety or effectiveness. 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 HALYCIL in patients with hepatic insufficiency. Since liver toxicity is associated with the use of propylthiouracil, caution is warranted in these patients. The dose should be kept as low as possible.

Renal impairment: No clinical studies have been performed with HALYCIL 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

HALYCIL 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. HALYCIL 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.

When a dose is missed, HALYCIL should be taken as soon as the missed dose is noted. However, if the next scheduled dose is close, the patient should wait and take the next scheduled dose; the missed dose should not be taken.

5 OVERDOSAGE

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

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. Overdose may manifest as vomiting, epigastric distress, headache, fever, arthralgia, pruritis and pancytopenia.

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.

The treatment of HALYCIL overdose should aim to minimise the amount of drug absorbed in the circulation. A full blood analysis should be considered because of the risk of haematological complications and appropriate therapy given if bone marrow depression develops.

Hemorrhage may be controlled by the administration of vitamin K1 and the dosage of HALYCIL should be reduced.

There is no specific antidote for propylthiouracil.

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, acacia spray-dried, croscarmellose sodium, sodium laurilsulfate, and magnesium stearate

Description

HALYCIL tablets are white, circular, biconvex tablets of approximately 6.5 mm by 3 mm. HALYCIL is supplied in bottles of 100 tablets or blister packs of 56 tablets.

7 WARNINGS AND PRECAUTIONS

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

General

HALYCIL 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 HALYCIL. 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 HALYCIL therapy.

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 HALYCIL therapy and initiate appropriate intervention.

Driving and Operating Machinery

HALYCIL has no or negligible influence on the ability to drive and use machines.

Endocrine and Metabolism

Hypothyroidism: HALYCIL 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 HALYCIL should be reduced or temporarily discontinued if signs of hypothyroidism occur during treatment.

Lactose: HALYCIL 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 is a potentially life-threatening side effect of HALYCIL therapy. Agranulocytosis typically occurs within the first few 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 immediately. Leukopenia, thrombocytopenia, and aplastic anemia (pancytopenia) may also occur.
HALYCIL 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: HALYCIL 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

Some cases of severe hepatic reaction resulting in liver failure, liver transplantation, or death, have 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. Time to onset has varied but in a majority of cases the liver reaction occurred within six months. 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 HALYCIL 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 HALYCIL should be employed.

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

Peri-Operative Considerations

When HALYCIL 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

HALYCIL should be used with caution in patients with renal impairment.

Reproductive Health: Female and Male Potential

Please see also **7.1.1 Pregnant Women**

- **Fertility**

  Hyperthyroidism can cause a marked reduction in sperm count resulting in infertility. Treatment with HALYCIL may result in normalisation in sperm count once the thyroid function is controlled.

  Hyperthyroidism can cause a reduction in fertility. Treatment with HALYCIL can result in rapid normalisation in fertility once the thyroid function is controlled. Women of childbearing potential should use effective methods of contraception during HALYCIL therapy and should be informed about the potential risks of HALYCIL use during pregnancy.
  See **7.1.1 Pregnant Women**

- **Teratogenic Risk**

  See section **7.1.1 Pregnant Women** below.

Respiratory

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

Skin

HALYCIL 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.
See **8 ADVERSE REACTIONS**

7.1 Special Populations

7.1.1 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 HALYCIL during pregnancy. If HALYCIL is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be warned of the potential hazard to the mother and fetus of liver damage.

HALYCIL can be used 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 HALYCIL.

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

HALYCIL, 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.

7.1.2 Breast-feeding

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

7.1.3 Pediatrics

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

7.1.4 Geriatrics

Geriatrics (>65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with no differences in safety or effectiveness.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most serious adverse reactions associated with HALYCIL 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.

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 HALYCIL. Typically, these reactions occur within the first two months of HALYCIL treatment. Injury is reversible upon discontinuation of HALYCIL 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 HALYCIL. HALYCIL-induced hepatotoxicity is not dose-related and is thought to be idiosyncratic with an autoimmune component.

Blood and Lymphatic System: Reversible leucopenia, agranulocytosis, thrombocytopenia, leucopenia aplastic anemia, pancytopenia; a rare complication of therapy is a tendency to hemorrhage associate with hypoprothrombinemia which may be controlled by the administration of vitamin K1.

Ear and Labyrinth Disorders: Hearing impairment may occur with HALYCIL. The impairment usually becomes less marked after withdrawal of the drug.

Gastrointestinal Disorders: Nausea, gastrointestinal disturbances, taste perversion, rarely vomiting.

General Disorders and Administration Site Conditions: Fever.

Hepatic Function: Jaundice (usually cholestatic), hepatic necrosis (sometimes with fatal consequences), encephalopathy, 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; hepatitis, hepatic failure.

Immune System Disorders: Interstitial pneumonitis, alveolar haemorrhage, lymphadenopathy, arthritis, nephritis, vasculitis and lupus erythematosus-like syndromes. There have also been rare reports of acute glomerulonephritis. Hypersensitivity reactions may also be associated with the development of antineutrophil cytoplasmic antibodies (ANCA).

Musculoskeletal and Connective Tissue Disorders: Myopathy, arthralgia.

Nervous System Disorders: Headache.

Skin and Subcutaneous Tissue Disorders: Papular skin rashes, pruritus, urticaria, alopecia, cutaneous vasculitis, serious hypersensitivity reactions. See **7 WARNINGS AND PRECAUTIONS**

8.5 Post-Market Adverse Reactions

Cases of congenital anomalies have been rarely reported in neonates whose mothers were treated with HALYCIL and other drugs during pregnancy. The pattern of congenital anomalies associated with HALYCIL is unclear, but may include anal atresia, accessory auricle, intestinal malrotation, gastrointestinal malformation and ventricular septal defect. See **7.1.1 Pregnant Women**

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Serious Drug Interactions

- Because HALYCIL 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 HALYCIL with agranulocytosis producing medication may increase the risk of agranulocytosis.

9.2 Drug Interactions Overview

Pre-treatment with HALYCIL 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 HALYCIL, 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 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.

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.

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 clinical response to propylthiouracil may be delayed for up to 2 weeks since the release of stored thyroid hormones is not affected.

10.2 Pharmacodynamics

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

10.3 Pharmacokinetics

Absorption: 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.

Distribution: Plasma half-life is 1-3 hours, the volume of distribution approximately 30 L with about 80% plasma binding. Propylthiouracil labelled with ^{35}S has been found to accumulate in the thyroid gland. It crosses the placental barrier and is found in the milk of nursing mothers.

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 - 25°C) in the original package in order to protect from light.

Keep this medicine out of the sight and reach of children.

12 SPECIAL HANDLING INSTRUCTIONS

None required.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

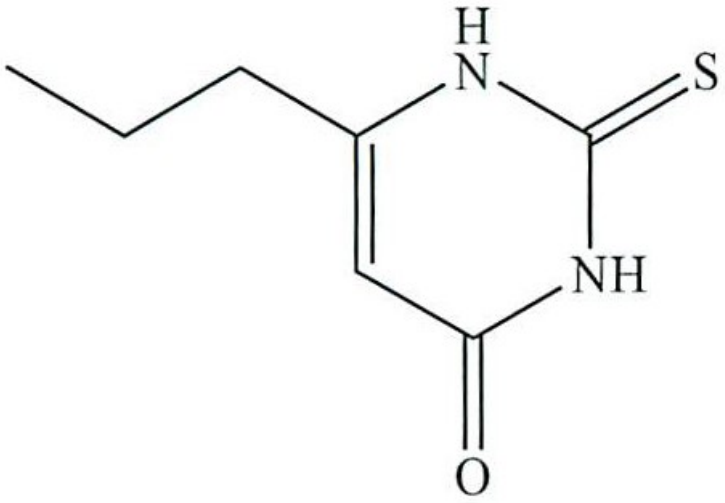
Drug Substance

Proper name: Propylthiouracil

Chemical name: 4(1H)-Pyrimidinone, 2,3,-dihydro-6-propyl-2-thioxo and 6-Propyl-2-thiouracil

Molecular formula and molecular mass: $C_7H_{10}N_2OS$ and 170.2 g/mol

Structural formula:



Physicochemical properties:

Description: Propylthiouracil contains not less than 98.0 percent and not more than the equivalent of 100.5 percent of 2,3-dihydro-6-propyl-2-thioxopyrimidin-4(1*H*)-one, calculated with reference to the dried substance.

Characters: White or almost white, crystalline powder or crystals, very slightly soluble in water, sparingly soluble in alcohol. It dissolves in solutions of alkali hydroxides.

Melting Point: 218 - 221°C

Acidity: pKa = 8.3 (20°C)

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

General Toxicology: 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.

17 SUPPORTING PRODUCT MONOGRAPHS

1. Halewood Chemicals Ltd. UK Summary of Product Characteristics, date of Revision 16/11/2019.
2. Prescribing Information for PrPROPYL-THYRACIL® Dated April 6, 2020 from Paladin Labs Inc. Control No. 233767

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr HALYCIL™

Propylthiouracil Tablets

Read this carefully before you start taking **HALYCIL™** 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 **HALYCIL™**.

Serious Warnings and Precautions

- **Agranulocytosis (low white blood cells):** Treatment with HALYCIL™ 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 HALYCIL™ 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 HALYCIL™ used for?

HALYCIL™ 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 hormones in a short period of time).

How does HALYCIL™ work?

HALYCIL™ 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 HALYCIL™?

Medicinal ingredient: propylthiouracil.

Non-medicinal ingredients: acacia spray-dried, croscarmellose sodium, lactose monohydrate, magnesium stearate and sodium laurilsulfate.

HALYCIL™ comes in the following dosage forms:

Tablets: 50 mg of propylthiouracil.

Do not use HALYCIL™ if:

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

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take HALYCIL™. 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 HALYCIL™);
- are taking an 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 HALYCIL™ 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 HALYCIL™ 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 HALYCIL™ can cause skin rashes. This can be a sign of an allergic reaction or a skin reaction. If you notice a skin rash stop taking HALYCIL™ right away and tell your healthcare professional.
- **Blood problems:** Treatment with HALYCIL™ 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 HALYCIL™.

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 HALYCIL™ is affecting you.

Pregnancy:

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

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

The following may interact with HALYCIL™:

- 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 HALYCIL™ 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 HALYCIL™ 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 HALYCIL™ 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 HALYCIL™:

- You can take HALYCIL™ 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 HALYCIL™.

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. Signs that you have taken too many tablets include vomiting, stomach pain, headache, fever, joint pain, itching, being pale, tiredness, frequent infections, unusual bleeding or unexplained bruising.

An overdose can also lead to the following:

- agranulocytosis (low white blood cells);
- hypothyroidism (thyroid gland is producing not enough thyroid hormone), in which case you may feel tired, cold, or put on weight.;
- hemorrhage (blood loss).

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

Missed Dose:

Do not take a double dose to make up for a missed dose. If you forget to take a dose, take it as soon as you remember. If it is almost time for your next dose, then do not take the missed dose at all. If you are not sure what to do, ask your healthcare professional.

What are possible side effects from using HALYCIL™?

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

Side effects may include:

- abdominal discomfort (vomiting, nausea, gastrointestinal disturbances);
- muscle and/or joint pain;
- drowsiness;
- burning or prickling sensation in the hands, arms, legs, or feet;
- loss of taste;
- hair loss;
- change in hair colour;
- mild skin rashes, itching or reddening of the skin;
- headaches;
- altered hearing.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your health 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 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)**:** fever, sore throat, rashes or ulcers in your mouth and throat, bruising, discomfort, unusual bleeding, infections, or chills			√
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			√

Serious side effects and what to do about them			
Symptom / effect	**Talk to your health professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
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: 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			√
Anemia (low red blood cells)**:** fatigue, loss of energy, irregular heartbeats, pale complexion, shortness of breath, and weakness			√
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 in your joints			√
Lupus-like syndrome: fever, joint swelling and pain, muscle aches, blood in urine, shortness of breath, or rash		√	
FREQUENCY UNKNOWN			
Severe skin reactions: a widespread rash with blisters and peeling skin around the mouth, nose, eyes and genitals, extensive peeling of the skin (more than 30% of the body), ulcers, or lesions			√

If you experience a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, consult with 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 HALYCIL™ at room temperature (15°C to 25°C) in the original package in order to protect from light.

Keep this medicine out of the sight and reach of children.

If you want more information about HALYCIL™:

- 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 (Halewood Chemicals Ltd.) website www.halewoodchemicals.com, the Canadian distributor's (Accelera Pharma Canada Inc.) website http://apcipharma.com/ or by calling 1-855-611-2724.

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