1.3.1.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Propylthiouracil Apotex 50 mg, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg propylthiouracil.

Excipient with known effect: 119.5 mg lactose per tablet.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Round white tablets, 9 mm in diameter, with a score line and inscription TAS-ZS.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hyperthyroidism.

4.2 Posology and method of administration

Posology
Due to the individual variation in absorption, it is recommended that the dosage be determined on the basis of hormone level tests. It is important to determine the lowest possible dosage to avoid the risk of hypothyroidism.

Adults
At the start of treatment, 1½-2 tablets 3 times per day (every 8 hours), if necessary 1½-2 tablets 4 times per day (every 6 hours) for 6-8 weeks.
Maintenance dose: ½-1 tablet 3 times per day (every 8 hours).
In the elderly, a lower dose is sometimes used.

Paediatric population
Children aged 10 to 12 years:
At the start of treatment, ½-1½ tablets 3 times per day (every 8 hours), if necessary ½-1½ tablets 4 times per day (every 6 hours) for 6-8 weeks.
Maintenance dose: ½ tablet 3 times per day (every 8 hours).

The initial dose is sometimes continued with the addition of thyroid hormones.

Method of administration
Take the tablets with a copious amount of water.
4.3 Contraindications
- hypersensitivity to propylthiouracil or to any of the excipients listed in section 6.1.
- tracheal obstruction
- severe hepatic impairment
- agranulocytosis during previous treatment with thiourea derivatives.

4.4 Special warnings and precautions for use

To obtain a good effect, it is important that the time interval between taking the tablets be strictly observed, i.e. every 8 hours or 6 hours exactly, depending on the prescription.

Onset of sore throat and/or fever may possibly be a symptom of agranulocytosis. It is therefore advisable not to prescribe other thiourea derivatives due to cross-hypersensitivity. Regular blood count monitoring is recommended during treatment.

Some cases of severe hepatic reactions, both in adults and in children, including fatal cases for which liver transplantation is necessary, have been reported with propylthiouracil. Time to onset varied, but in the majority of cases, the hepatic reaction occurred within 6 months. If there are significant enzyme abnormalities during treatment with propylthiouracil, use of the medicinal product must be discontinued immediately (see section 4.8).

This product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

As antithyroid agents affect the metabolism, adjustment of the dose of other medicinal products may be required.

4.6 Pregnancy and lactation

Pregnancy
Propylthiouracil crosses the placenta and is excreted in human milk.
In general, propylthiouracil is regarded as the agent of first choice in hyperthyroidism during pregnancy. It is essential to use the lowest possible dose of propylthiouracil during pregnancy and to accurately assess thyroid function in the neonate.
Treatment reduces the risk of premature birth as a result of hyperthyroidism. Treatment during pregnancy should take place only under close supervision by the specialist.

Breastfeeding
Breastfeeding during treatment is not recommended.

4.7 Effects on ability to drive and use machines

No known data.

4.8 Undesirable effects

The following adverse reactions may occur:
- hypothyroidism and goitre
- allergic reactions, such as skin rash and pruritus
- sore throat and/or fever (see section 4.4)
- headache
  - alopecia
  - myalgia and arthralgia
  - exophthalmos
  - nausea
  - loss of taste
  - cholestatic jaundice
  - aplastic anaemia

Rare (less than 1% of cases): agranulocytosis, leukopenia and thrombocytopenia.

Frequency not known: hepatitis, liver failure.

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Nederlands Bijwerkingen Centrum Lareb (Dutch Pharmacovigilance Centre Lareb), website: [www.lareb.nl](http://www.lareb.nl).

### 4.9 Overdose

Overdose will cause symptoms of hypothyroidism.
Treatment should primarily consist of discontinuing or reducing the propylthiouracil treatment. An alternative method is to maintain the propylthiouracil dosage and to supplement T4 until the symptoms of hypothyroidism have resolved. This technique is sometimes used as therapy for hyperthyroidism when severe exophthalmos is also present. Here, too, regular testing of hormone levels is recommended.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antithyroid agents  
ATC code: H03BA02

Thiourea derivatives inhibit the iodination of thyroglobulin in the thyroid gland and thus reduce the synthesis of liothyronine (T3) and levothyroxine (T4). At the usual dosage, they have no influence on already formed thyroid hormone. Furthermore, propylthiouracil inhibits the peripheral conversion of T4 to T3.  
Propylthiouracil interferes with oxidation of the iodide ion - and oxidative coupling between iodinated tyrosyl groups and thyroglobulin within the thyroid gland - via inhibition of the peroxidase enzyme in the thyroid. Ultimately, inhibition of synthesis leads to a depletion of liothyronine (T3) and levothyroxine (T4). This means that a latency time for efficacy occurs. This latency time can vary from a few days to weeks, depending on thyroid status. The ultimate effect of propylthiouracil on the peripheral conversion of T4 to T3, a second mechanism of action, is unclear.

### 5.2 Pharmacokinetic properties

**Absorption**

In general, propylthiouracil is rapidly absorbed. Peak plasma levels are reached within 1-1.5 hours. In the literature, however, food intake is reported to delay uptake and decrease absorption (see also Posology). Plasma protein binding is approximately 80%.
Elimination
Propylthiouracil has a shorter duration of action than carbimazole and thiamazole as a result of a shorter half-life (1-2 hours for propylthiouracil vs. 6-13 hours for carbimazole and thiamazole). 35% is excreted with the urine within 24 hours as a metabolite or in unchanged form. Clearance of propylthiouracil in the elderly is unchanged.

5.3 Preclinical safety data
None.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose
Magnesium stearate
Maize starch
Sodium starch glycolate type A
Colloidal silica anhydrous
Pregelatinised maize starch
Talc

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
5 years.

6.4 Special precautions for storage
Store below 25°C.

6.5 Nature and contents of container
PVC/aluminium blisters of 30 and 50 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.
7. MARKETING AUTHORISATION HOLDER

Apotex Europe BV
Darwinweg 20
2333 CR Leiden
Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

RVG 52546 Propylthiouracil Apotex 50 mg, tablets

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27 May 1992

10. DATE OF REVISION OF THE TEXT

Latest complete revision: 29 May 2013