associated with serious dose-related adverse effects. Aplastic anaemia (with some fatalities), agranulocytosis, leucopenia, pancytopenia, and the nephrotic syndrome have been reported. Excessive doses may cause hypothyroidism and goitre.

Effects on the blood. There have been reports of fatal aplastic anaemia[1,2] and of leucopenia and agranulocytosis[1] associated with the use of potassium perchlorate for the treatment of hyperthyroidism. A review[3] in 1998 noted that despite an increase in perchlorate use in recent years there did not appear to have been any further cases of aplastic anaemia since the 1960s.

1. Anonymous. Potassium perchlorate and aplastic anaemia. *BMJ* 1961; **i:** 1520–1.
2. Krevans JR, *et al*. Fatal aplastic anemia following use of potassium perchlorate in thyrotoxicosis. *JAMA* 1962; **181:** 182–4.
3. Wolff J. Perchlorate and the thyroid gland. *Pharmacol Rev* 1998; **50:** 89–105.

Uses and Administration

Potassium and sodium perchlorate reduce the uptake and concentration of iodide, pertechnetate, and other anions by the thyroid, choroid plexus, gastric mucosa, and salivary glands, probably by competitive inhibition of active transport mechanisms.

They are used **diagnostically** as adjuncts to pertechnetate (^{99m}Tc) to enhance visualisation of the brain, Meckel's diverticulum, or the placenta by reducing unwanted images of other organs. The usual oral dose of either potassium or sodium perchlorate is 200 to 400 mg given 30 to 60 minutes before the use of sodium pertechnetate (^{99m}Tc).

Potassium and sodium perchlorate are also used with sodium iodide (^{131}I) in the perchlorate discharge test of thyroid function. The release of radio-iodine from the gland following an oral dose of perchlorate indicates a defect in the binding of iodide by the thyroid and thus a defect in thyroid hormone synthesis. The test has also been used to investigate the action of antithyroid drugs.

Potassium and sodium perchlorate have been used in the treatment of **hyperthyroidism** (p.2165), but because of toxicity have been largely replaced by alternative treatments. However, perchlorates may be useful in patients with iodine-induced hyperthyroidism such as that associated with amiodarone therapy, by increasing responsiveness to conventional antithyroid drugs. A typical dose of potassium perchlorate in amiodarone-induced hyperthyroidism is 1 g daily.

◊ References.

1. Bartalena L, *et al*. Treatment of amiodarone-induced thyrotoxicosis, a difficult challenge: results of a prospective study. *J Clin Endocrinol Metab* 1996; **81:** 2930–3.
2. Wolff J. Perchlorate and the thyroid gland. *Pharmacol Rev* 1998; **50:** 89–105.
3. Soldin OP, *et al*. Perchlorate clinical pharmacology and human health: a review. *Ther Drug Monit* 2001; **23:** 316–31.
4. Bartalena L, *et al*. Diagnosis and management of amiodarone-induced thyrotoxicosis in Europe: results of an international survey among members of the European Thyroid Association. *Clin Endocrinol (Oxf)* 2004; **61:** 494–502.

Preparations

USP 31: Potassium Perchlorate Capsules.

Proprietary Preparations (details are given in Part 3)
Austria: Irenat; ***Cz.:*** Irenat; ***Ger.:*** Irenat; ***Ital.:*** Pertiroid; ***Pol.:*** Irenat; ***USA:*** Perchloracap†.

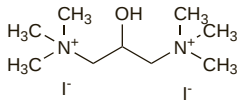
Prolonium Iodide *(rINN)*

Ioduro de prolonio; Prolonii Iodidum; Prolonium, Iodure de. *NN*-(2-Hydroxytrimethylene)bis(trimethylammonium) di-iodide.

Пролония Йодид

$C_9H_{24}I_2N_2O$ = 430.1.

CAS — 123-47-7.



Pharmacopoeias. In *Chin.*

Profile

Prolonium iodide has been given by injection as a source of iodine (p.2169) as part of the treatment of thyroid storm and for the pre-operative management of hyperthyroidism.

Propylthiouracil *(BAN, rINN)*

Proiltiourasil; Propiltiouracil; Propiltiouracilas; Propiltiouracilo; Propylthiouracile; Propylthiouracilum; Propyltiouracil; Propyylitiourasiili. 2,3-Dihydro-6-propyl-2-thioxopyrimidin-4(1*H*)-one; 2-Mercapto-6-propylpyrimidin-4-ol; 6-Propyl-2-thiouracil.

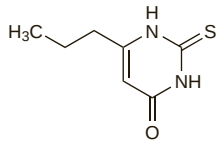
Пропилтиоурацил

$C_7H_{10}N_2OS$ = 170.2.

CAS — 51-52-5.

ATC — H03BA02.

ATC Vet — QH03BA02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Propylthiouracil). White or almost white crystals or crystalline powder. Very slightly soluble in water; sparingly soluble in alcohol; dissolves in solutions of alkali hydroxides. Protect from light.
USP 31 (Propylthiouracil). A white, powdery, crystalline substance. It is starch-like in appearance and to the touch. Slightly soluble in water, in chloroform, and in ether; sparingly soluble in alcohol; soluble in ammonium hydroxide and in alkali hydroxides. Protect from light.

Adverse Effects and Precautions

As for Carbimazole, p.2167, although cross-sensitivity to carbimazole does not necessarily occur.

Propylthiouracil has been associated with greater hepatotoxicity than other thiourea antithyroid drugs (such as carbimazole or thiamazole). Rarely hepatitis, hepatic necrosis, encephalopathy, and death have occurred; asymptomatic liver damage is more common (see Effects on the Liver, under Carbimazole, p.2168).

Propylthiouracil should be given with care, and in reduced doses, to patients with renal impairment.

Breast feeding. Propylthiouracil has been preferred to carbimazole or thiamazole since it enters breast milk less readily, see Breast Feeding, under Carbimazole, p.2167.

Pharmacokinetics

Propylthiouracil is rapidly absorbed from the gastrointestinal tract with a 50 to 75% bioavailability and with peak plasma concentrations occurring about 2 hours after oral doses. It is concentrated in the thyroid gland; since its duration of action is more closely related to the intrathyroidal drug concentration than its plasma half-life, prolonged antithyroid activity results from single daily doses. Propylthiouracil is about 80% bound to plasma proteins.

Propylthiouracil has an elimination half-life of about 1 to 2 hours. It undergoes rapid first-pass metabolism in the liver, and is mainly excreted in the urine as the glucuronic acid conjugate, with less than 2% excreted as unchanged drug. The elimination half-life may be increased in renal or hepatic impairment.

Propylthiouracil crosses the placenta and is distributed into breast milk.

Uses and Administration

Propylthiouracil is a thiourea antithyroid drug that acts by blocking the production of thyroid hormones (see p.2165); it also inhibits the peripheral deiodination of thyroxine to tri-iodothyronine. It is used in the management of hyperthyroidism (p.2165), including the treatment of Graves' disease, preparation of hyperthyroid patients for thyroidectomy, use as an adjunct to radioiodine therapy, and the treatment of thyroid storm.

Propylthiouracil is usually given orally. Initial doses range from 150 to 450 mg daily (the *BNF* recommends 200 to 400 mg daily), although in severe cases initial doses of 600 to 1200 mg daily have been used. It has often been given in divided daily doses but once daily dosage is also possible. Improvement is usually seen in 1 to 3 weeks and control of symptoms is achieved in 1 to 2 months. When the patient is euthyroid the dose is gradually reduced to a maintenance dose, usually 50 to 150 mg daily. Treatment is usually continued for 1 to 2 years. In the UK, the *BNFC* recommends the following initial doses by mouth for children:

- in neonates: 2.5 to 5 mg/kg twice daily
- in those aged 1 month to 1 year: 2.5 mg/kg three times daily
- in those aged 1 to 5 years: 25 mg three times daily
- in those aged 5 to 12 years: 50 mg three times daily
- in those aged 12 to 18 years: 100 mg three times daily

These doses are given until the patient is euthyroid and then adjusted as needed; higher doses may be required, especially in thyrotoxic crises.

Doses should be reduced in renal impairment (below). Doses may also need to be reduced in hepatic impairment.

Administration in renal impairment. The dosage of propylthiouracil should be reduced in patients with renal impairment according to creatinine clearance (CC) as follows:

- CC 10 to 50 mL/minute, doses should be reduced by 25%
- CC less than 10 mL/minute, reduce doses by 50%

Alcoholic liver disease. Propylthiouracil has been said to reduce hyperoxic liver injury in hypermetabolic *animals* and despite reports of hepatotoxicity, including some fatalities, associated with propylthiouracil (see Effects on the Liver, under Carbimazole, p.2168), it has been investigated in the treatment of patients with alcoholic liver disease. A systematic review[1], however, concluded that there is no evidence to substantiate this use. Propylthiouracil was associated with adverse effects and it could not be shown to have any significant effects on mortality, liver related mortality, liver complications, and liver histology.

1. Rambaldi A, Gluud C. Propylthiouracil for alcoholic liver disease. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 01/08/08).

Psoriasis. Several reports have described benefit in patients with psoriasis (p.1583) given propylthiouracil. An oral dose of 300 mg daily for 8 to 12 weeks has been used and is said not to produce clinical hypothyroidism.[1]

1. Elias AN. Anti-thyroid thioureylenes in the treatment of psoriasis. *Med Hypotheses* 2004; **62:** 431–7.

Preparations

BP 2008: Propylthiouracil Tablets;
USP 31: Propylthiouracil Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Prothiucil; ***Braz.:*** Propil; Propilracil; ***Canad.:*** Propyl-Thyracil; ***Cz.:*** Propycil; ***Ger.:*** Propycil; Thyreostat II†; ***Gr.:*** Prothuril; ***Hong Kong:*** CP-PTU; ***Hung.:*** Propycil; ***Israel:*** Propylthiocil; ***Pol.:*** Thyrosan; ***Port.:*** Propycil; ***Swed.:*** Tiotil; ***Switz.:*** Propycil; ***Thai.:*** Propyl; Uracil; ***Turk.:*** Propycil.

Protirelin *(BAN, USAN, rINN)*

Abbott-38579; Lopremone; Protireliini; Protirelina; Protirelinas; Protiréline; Protirelinum; Synthetic TRH; Thyrotrophin-releasing Hormone; Thyrotropin-releasing Hormone; TRF; TRH. L-Pyroglutamyl-L-histidyl-L-prolinamide; 1-[*N*-(5-Oxo-L-prolyl)-L-histidyl]-L-prolinamide; Glu-His-Pro-NH_2.

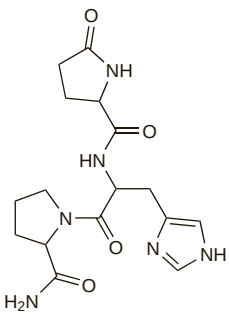
Протирелин

$C_{16}H_{22}N_6O_4$ = 362.4.

CAS — 24305-27-9.

ATC — V04CJ02.

ATC Vet — QV04CJ02.



Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*, which also includes the tartrate.
Ph. Eur. 6.2 (Protirelin). A synthetic tripeptide with the same sequence of amino acids as the natural hypothalamic neurohormone, that stimulates the release and synthesis of thyrotrophin.

A white or yellowish-white hygroscopic powder. Very soluble in water; freely soluble in methyl alcohol. Store at a temperature of 2° to 8°. Protect from light and moisture.

Adverse Effects

Protirelin given by intravenous injection may cause headache, nausea, a desire to micturate, flushing, dizziness, and a strange taste. These effects have been attributed to contraction of smooth muscles by the bolus injection. Hypertension and an increased pulse rate, or hypotension, have occasionally been reported as have a few cases of amaurosis and convulsions.

Amaurosis. Of 4 patients with pituitary tumours who developed severe headache after protirelin injection, one also developed amaurosis, apparently associated with pituitary apoplexy.[1] Visual acuity improved after surgery.

1. Drury PL, *et al.* Transient amaurosis and headache after thyrotropin releasing hormone. *Lancet* 1982; **i:** 218–19.

Effects on the cardiovascular system. Increased blood pressure has been reported in women given protirelin antenatally,[1,2] and the view has been expressed that although the magnitude of the change is unlikely to be clinically significant in normotensive women, much greater rises have been seen in pre-eclamptic women[2,3] and may be severe enough to increase the risk of cerebral haemorrhage.[2]

1. ACTOBAT Study Group. Australian collaborative trial of antenatal thyrotropin-releasing hormone (ACTOBAT) for prevention of neonatal respiratory disease. *Lancet* 1995; **345:** 877–82.
2. Peek MJ, *et al.* Hypertensive effect of antenatal thyrotropin-releasing hormone in pre-eclampsia. *Lancet* 1995; **345:** 793. Correction. *ibid.*; 1124.
3. Tan ASA, *et al.* Is maternal thyrotropin releasing hormone administration safe in the pregnant women with preeclampsia? *Am J Perinatol* 1997; **14:** 5–6.

Effects on the CNS. Adverse effects reported after injection of 400 micrograms of protirelin included unconsciousness, hypotension, and convulsions.[1] In another patient with a history of convulsions, a 500-microgram injection induced epileptic seizures.[2]

1. Dolva LØ, *et al.* Side effects of thyrotrophin releasing hormone. *BMJ* 1983; **287:** 532.
2. Maeda K, Tanimoto K. Epileptic seizures induced by thyrotropin releasing hormone. *Lancet* 1981; **i:** 1058–9.

Effects on the respiratory system. Bronchospasm occurred in an asthmatic boy given protirelin intravenously.[1]

For a report that protirelin provoked bronchospasm in patients with motor neurone disease, see under Precautions, below.

1. McFadden RG, *et al*. TRH and bronchospasm. *Lancet* 1981; **ii:** 758–9.

Effect on sexual function. On questioning, 7 of 16 women reported a sensation of mild vaginal sexual arousal occurring 1 to 3 minutes after intravenous injection of protirelin.[1] Four women also had urinary sensations, and 3 described an urge to urinate with no sexual component.

1. Blum M, Pulini M. Vaginal sensations after injection of thyrotropin releasing hormone. *Lancet* 1980; **ii:** 43.

Pituitary apoplexy. Pituitary apoplexy has been reported after combined testing of anterior pituitary function in patients with a pituitary tumour.[1,2] Of the drugs given, protirelin was thought most likely to have an aetiological role. Pituitary apoplexy has also been reported after the use of protirelin alone.[3]

See also Amaurosis, above.

1. Chapman AJ, *et al*. Pituitary apoplexy after combined test of anterior pituitary function. *BMJ* 1985; **291:** 26.
2. Dökmetaş HS, *et al*. Pituitary apoplexy probably due to TRH and GnRH stimulation tests in a patient with acromegaly. *J Endocrinol Invest* 1999; **22:** 698–700.
3. Szabolcs I, *et al.* Apoplexy of a pituitary macroadenoma as a severe complication of preoperative thyrotropin-releasing hormone (TRH) testing. *Exp Clin Endocrinol Diabetes* 1997; **105:** 234–6.

Precautions

Protirelin should be given with care to patients with ischaemic heart disease, obstructive airways disease, or severe hypopituitarism. Giving protirelin while the patient is lying down may reduce the incidence of hypotension.

Eclampsia. For the suggestion that the hypertensive effects of protirelin increase the risk of cerebral haemorrhage in pre-eclamptic women, see Effects on the Cardiovascular System under Adverse Effects, above.

Motor neurone disease. In some patients with amyotrophic lateral sclerosis, intravenous injection of protirelin resulted in acute bronchospasm.[1] Five of 25 patients had falls in FEV_1 of more than 20%; in 2, a 15% decrease in arterial-oxygen pressure occurred. Patients with sclerosis and weakened respiratory muscles should be warned of this potential adverse effect.

1. Braun SR, *et al*. Pulmonary effects of thyrotropin-releasing hormone in amyotrophic lateral sclerosis. *Lancet* 1984; **ii** 529–30.

Interactions

◊ Drugs influencing the response to protirelin have been reviewed.[1] The secretion of thyrotrophin appears to be modulated by dopaminergic and noradrenergic pathways at both the hypothalamic and pituitary level. Dopamine and bromocriptine have depressed the response to protirelin; levodopa is a powerful depressant. Partial depression has been reported after the use of chlorpromazine, thioridazine, and phentolamine, all of which have alpha-receptor blocking properties. Beta-receptors do not appear to be involved in the thyrotrophin response to protirelin whereas the antiserotonin drug, cyproheptadine, has an inhibitory effect. Aspirin and corticosteroids with mainly glucocorticoid activity have also depressed the response. An enhanced response to protirelin has been seen after theophylline. Oestrogens may also increase the response in men but not usually in women; when combined with a progestogen a slightly depressed response has been reported.

Other drugs reported to depress the response to protirelin include lithium[2] and ranitidine.[3]

1. Lamberg B-A, Gordin A. Abnormalities of thyrotrophin secretion and clinical implications of the thyrotrophin releasing hormone stimulation test. *Ann Clin Res* 1978; **10:** 171–83.
2. Lauridsen UB, *et al.* Lithium and the pituitary-thyroid axis in normal subjects. *J Clin Endocrinol Metab* 1974; **39:** 383–5.
3. Tarditi E, *et al.* Impaired TSH response to TRH after intravenous ranitidine in man. *Experientia* 1983; **39:** 109–10.

Uses and Administration

Protirelin is a hypothalamic releasing hormone that stimulates the release of thyrotrophin (p.2177) from the anterior lobe of the pituitary. It also has prolactin-releasing activity. It may be obtained by synthesis.

Protirelin may be used in the assessment of the hypothalamic-pituitary-thyroid axis in the diagnosis of mild hyperthyroidism (p.2165) or hypothyroidism (p.2167), and ophthalmic Graves' disease, although in many cases immunoassays for thyroid-stimulating hormone are now preferred. The response to protirelin may be used for differentiating between primary and secondary hypothyroidism but care is required in interpreting the results of the test and it should not be used alone in establishing the diagnosis. Protirelin is given with gonadorelin (p.2107) in the assessment of anterior pituitary function.

Protirelin is given intravenously, usually in doses of 200 to 400 micrograms. A suggested intravenous dose in children is 1 microgram/kg for the assessment of thyroid function. The *BNFC* gives a dose of 7 micrograms/kg (to a maximum of 200 micrograms) for the diagnosis of hypopituitarism and hypothalamic disease.

Protirelin has been investigated in the treatment of neurological diseases, and in the prevention of neonatal respiratory distress syndrome, but results have been variable.

Protirelin tartrate has been given in the treatment of neurological disorders.

Lactation induction. Intranasal protirelin has been tried for stimulation of lactation (p.2003) but there is no suitable commercial preparation, and in any case mechanical stimulation is preferable to drug treatment.

Neonatal respiratory distress syndrome. The regulation of fetal lung development is under multihormonal control and thyroid hormones appear to stimulate pulmonary maturation. However, the thyroid hormones and thyrotrophin do not cross the placenta sufficiently for them to be given in premature labour where neonatal respiratory distress syndrome (p.1508) may develop; therapy with protirelin has therefore been investigated.[1]

Protirelin has been given with corticosteroids to the mother and some beneficial effects have been noted.[1] One study using protirelin 400 micrograms every 8 hours for 4 doses indicated that antenatal protirelin reduced the incidence of chronic lung disease when given with corticosteroids but did not affect the incidence of respiratory distress syndrome.[2] However, 2 large multicentre studies had found that addition of protirelin to corticosteroid treatment had no beneficial effects on outcome compared with corticosteroids only;[3,4] in fact, in the earlier of these studies,[3] respiratory distress syndrome and the need for ventilation were greater in the offspring of mothers given protirelin. Subsequent follow-up appeared to confirm the disadvantages of protirelin in this cohort;[5] however the unexpected conclusions of this study aroused some controversy.[6-8] The second study noted no difference in outcome in the 2 groups of infants.[4] A meta-analysis concluded[9] that prenatal treatment with protirelin was not beneficial, and that it was associated with more adverse effects than the use of corticosteroids alone.

1. de Zegher F, *et al.* Prenatal treatment with thyrotrophin releasing hormone to prevent neonatal respiratory distress. *Arch Dis Child* 1992; **67:** 450–4.
2. Ballard RA, *et al.* Respiratory disease in very-low-birthweight infants after prenatal thyrotropin-releasing hormone and glucocorticoid. *Lancet* 1992; **339:** 510–5.
3. ACTOBAT Study Group. Australian collaborative trial of antenatal thyrotropin-releasing hormone (ACTOBAT) for prevention of neonatal respiratory disease. *Lancet* 1995; **345:** 877–82.
4. Ballard RA, *et al.* Antenatal thyrotropin-releasing hormone to prevent lung disease in preterm infants. *N Engl J Med* 1998; **338:** 493–8.
5. Crowther CA, *et al.* Australian collaborative trial of antenatal thyrotropin-releasing hormone: adverse effects at 12-month follow-up. *Pediatrics* 1997; **99:** 311–17.
6. Ballard RA, *et al.* Thyrotropin-releasing hormone for prevention of neonatal respiratory disease. *Lancet* 1995; **345:** 1572.
7. Moya FR, Maturana A. Thyrotropin-releasing hormone for prevention of neonatal respiratory disease. *Lancet* 1995; **345:** 1572–3.
8. McCormick MC. The credibility of the ACTOBAT follow-up study. *Pediatrics* 1997; **99:** 476–8.
9. Crowther CA, *et al.* Thyrotropin-releasing hormone added to corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2004 (accessed 16/09/05).

Neurological disorders. Reports of the use of protirelin in various neurological disorders.

1. Bonuccelli U, *et al.* Oral thyrotropin-releasing hormone treatment in inherited ataxias. *Clin Neuropharmacol* 1988; **11:** 520–8.
2. Filla A, *et al.* Sperimentazione cronica del TRH per via intramuscolare nelle degenerazioni spino-cerebellari: studio in doppio cieco cross-over su 30 soggetti. *Riv Neurol* 1989; **59:** 83–8.
3. Mellow AM, *et al.* A peptide enhancement strategy in Alzheimer's disease: pilot study with TRH-physostigmine infusions. *Biol Psychiatry* 1993; **34:** 271–3.
4. Chemaly R, *et al.* Myélinolyse extra-pontine: traitement par T.R.H. *Rev Neurol (Paris)* 1998; **154:** 163–5.
5. Tzeng AC, *et al.* A study of thyrotropin-releasing hormone for the treatment of spinal muscular atrophy: a preliminary report. *Am J Phys Med Rehabil* 2000; **79:** 435–40.
6. Kubek MJ, Garg BP. Thyrotropin-releasing hormone in the treatment of intractable epilepsy. *Pediatr Neurol* 2002; **26:** 9–17.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: TRH; Trhelea; ***Austria:*** Antepan; Relefact TRH; Thyroliberin TRH†; ***Belg.:*** TRH; ***Braz.:*** TRH†; ***Canad.:*** Relefact TRH; ***Cz.:*** TRH†; ***Fr.:*** Stimu-TSH; ***Ger.:*** Antepan; Relefact TRH†; Thyroliberin; TRH; ***Gr.:*** Relefact†; TRH; ***Israel:*** Relefact TRH; TRH; ***Ital.:*** Irtonin†; Xantium†; ***Jpn:*** Hirtonin; ***Neth.:*** Relefact TRH; ***Spain:*** TRH Prem; ***Switz.:*** Relefact TRH†; ***Turk.:*** TRH.

Thiamazole *(BAN, rINN)*

Mercazolylum; Methimazole; Methylmercaptoimidazole; Metimazol; Thiamazol; Thiamazolum; Tiamatsoli; Tiamazol; Tiamazolas. 1-Methylimidazole-2-thiol.

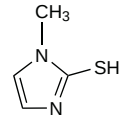
Тиамазол

$C_4H_6N_2S$ = 114.2.

CAS — 60-56-0.

ATC — H03BB02.

ATC Vet — QH03BB02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US.*

Ph. Eur. 6.2 (Thiamazole). A white or pale brown, crystalline powder. Freely soluble in water and in dichloromethane; freely soluble or soluble in alcohol.

USP 31 (Methimazole). A white to pale buff crystalline powder having a faint characteristic odour. Soluble 1 in 5 of water, 1 in 5 of alcohol, 1 in 4.5 of chloroform, and 1 in 125 of ether. Its solutions are practically neutral to litmus. Protect from light.

Adverse Effects and Precautions

As for Carbimazole, p.2167.

Breast feeding. The use of thiamazole during breast feeding is discussed under Carbimazole, p.2167.

Pharmacokinetics

The pharmacokinetics of thiamazole can be considered with those of carbimazole (p.2168) since the latter is rapidly and completely metabolised to thiamazole in the body.