

Uses and Administration

Thiamazole is a thiourea antithyroid drug that acts by blocking the production of thyroid hormones (see p.2165). It is used in the management of hyperthyroidism (p.2165), including the treatment of Graves' disease, the preparation of hyperthyroid patients for thyroidectomy, use as an adjunct to radio-iodine therapy, and the treatment of thyroid storm.

Thiamazole is given orally usually in an initial dosage of 15 to 60 mg daily. It is usually given in three divided doses but a single daily dose is also possible. Improvement is usually seen in 1 to 3 weeks and control of symptoms in 1 to 2 months. When the patient is euthyroid the dose is gradually reduced to a maintenance dose, usually 5 to 15 mg daily. Alternatively, the dose may be continued at the initial level with supplemental levothyroxine as a *blocking-replacement regimen*. Either form of maintenance treatment is usually continued over 1 to 2 years. The initial dose for children is 400 micrograms/kg daily in 3 divided doses; for maintenance this dose may be halved.

Thiamazole doses of 80 to 240 mg daily, usually in 3 or 4 divided doses, have been given intravenously in the management of thyroid storm.

Preparations

USP 31: Methimazole Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Danantizol; **Austria:** Favistan†; **Belg.:** Strumazol; **Braz.:** Tapazol; **Canada:** Tapazole; **Chile:** Thyrozol; Tirozol 5/10†; **Cz.:** Favistan†; Thyrozol; **Denm.:** Thyrapzol; **Ger.:** Favistan; Thyrozol; **Gr.:** Unimazole; **Hung.:** Metiothylin; **Indon.:** Thyrozol; **Israel:** Mercapitol; **Ital.:** Tapazole; **Mex.:** Tapazol; **Neth.:** Strumazol; **Philipp.:** Strumazol; Tapazole; **Pol.:** Metioz; Thyrozol; **Port.:** Metibazol; **Rus.:** Mercazolil (Мерказолил); Thyrozol (Тирозол); **Singapore:** Thyrozol; **Spain:** Tirodri†; **Swed.:** Thacapzol; **Switz.:** Tapazole†; **Thai.:** Tapazole; Timazol; **Turk.:** Thyromazol; **USA:** Northx; Tapazole; **Venez.:** Tapazol.

Multi-ingredient: **Ital.:** Bromazolol.

Thyroglobulin (USAN, rINN)

Thyroglobuline; Thyroglobulinum; Tiroglobulina.

Тироглобулин
CAS — 9010-34-8.

Profile

Thyroglobulin is an extract obtained by the fractionation of porcine thyroid glands, that yields levothyroxine and liothyronine on hydrolysis. It has been used in the treatment of hypothyroidism, but such treatment with mixtures of thyroid hormones or preparations of animal extracts is not recommended.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Tiroide Vister.

Thyroid

Dry Thyroid; Getrocknete Schilddrüse; Glándula tiroides, extracto de; NSC-26492; Thyroidin; Thyroid Extract; Thyroid Gland; Thyroidea; Thyroideum Siccum; Tiroide Secca.

ATC — H03AA05.
ATC Vet — QH03AA05.

Pharmacopoeias. In *Chin., Jpn., and US.*

USP 31 (Thyroid). It is the cleaned, dried, and powdered thyroid gland, previously deprived of connective tissue and fat, obtained from domesticated animals used for food by humans. On hydrolysis it yields not less than 90% and not more than 110% each of the labelled amounts of levothyroxine and liothyronine calculated on the dried basis. It is free from iodine in inorganic or any form of combination other than that peculiar to the thyroid gland. It may contain a suitable diluent such as glucose, lactose, sodium chloride, starch, or sucrose. A yellowish to buff-coloured amorphous powder, having a slight, characteristic, meat-like odour. Store in airtight containers.

Profile

Thyroid has been used in the treatment of hypothyroidism, but treatment with mixtures of thyroid hormones or preparations of animal extracts is not recommended.

Preparations

USP 31: Thyroid Tablets.

Proprietary Preparations (details are given in Part 3)

Ital.: Cinetic; **Mex.:** Amet; **Thai.:** Thyroid; **USA:** Nature Thyroid.

Multi-ingredient: **Braz.:** Emagrex†; Obesidex†; Obesifran†; **India:** Ebexid; **Thai.:** Metharmon-F.

Thyrotrophin (BAN, rINN)

Thyroid-stimulating Hormone; Thyrotrophic Hormone; Thyrotrophine; Thyrotrophinum; Thyrotropin; Thyrotropinum; Tirotrófina; TSH; Thyrotropini; Thyrotropin.

Тиротропин

CAS — 9002-71-5.
ATC — H01AB01; V04CJ01.
ATC Vet — QH01AB01; QV04CJ01.

Description. Thyrotrophin is a glycoprotein from the anterior pituitary with a molecular weight in man of about 30 000.

Thyrotrophin Alfa (BAN, USAN, rINN)

rhTSH; Thyrotropine Alfa; Thyrotropinum Alfa; Tirotrófina alfa.

Тиротропин Альфа

CAS — 194100-83-9.
ATC — V04CJ01.
ATC Vet — QV04CJ01.

Units

0.037 units of human pituitary thyrotrophin for immunoassay and bioassay are contained in about 7.5 micrograms of thyrotrophin, with albumin 1 mg and lactose 5 mg, in one ampoule of the second International Reference Preparation (1983).

Adverse Effects

Infrequent adverse effects of thyrotrophin include nausea, vomiting, headache, a desire to micturate, and flushing. High doses may produce excessive thyroid stimulation, with angina, tachycardia or arrhythmias, dyspnoea, sweating, nervousness and irritability. Hypersensitivity reactions, including skin rash and urticaria, erythema and swelling at the injection site, and anaphylaxis have occurred, particularly on repeated use.

Precautions

Thyrotrophin should not be given to patients with recent myocardial infarction or uncorrected adrenocortical insufficiency, including adrenocortical insufficiency secondary to hypopituitarism. Care is also required in patients with cardiovascular disease.

Uses and Administration

Thyrotrophin is a glycoprotein that is secreted by the anterior lobe of the pituitary and has an alpha subunit essentially the same as that of the gonadotrophins. Its main actions are to increase iodine uptake by the thyroid and the formation and secretion of the thyroid hormones. It may produce hyperplasia of thyroid tissue. Thyrotrophin secretion is controlled by a hypothalamic releasing hormone (Protirelin, p.2175) and by circulating thyroid hormones; somatostatin (p.1809) inhibits the release of thyrotrophin. Thyrotrophin has been used with radio-iodine in the diagnosis of hypothyroidism (p.2167) and to differentiate between primary and secondary hypothyroidism, but direct radio-immunoassay of circulating endogenous thyroid-stimulating hormone may be preferred. Thyrotrophin increases the uptake of radio-iodine by the thyroid and has been used as a diagnostic tool and as an adjunct in the treatment of certain types of thyroid cancer.

Thyrotrophin alfa is a recombinant form of thyrotrophin used as an adjunctive diagnostic tool for serum-thyroglobulin testing, with or without radio-iodine imaging, in the follow-up of patients with thyroid cancer. It is also used to increase radio-iodine uptake for ablation of thyroid remnant tissue after thyroidectomy. The usual thyrotrophin alfa regimen consists of 2 intramuscular doses of 900 micrograms given 24 hours apart. Radio-iodine is given 24 hours after the second dose of thyrotrophin alfa for radio-iodine imaging or remnant ablation. Diagnostic scanning is performed 48 to 72 hours after the radio-iodine has been given, but post-therapy scanning may be delayed by additional days to allow background activity to decline. Samples for serum-thyroglobulin testing should be taken 72 hours after the second thyrotrophin alfa dose.

Goitre and thyroid nodules. Thyrotrophin alfa is under investigation¹⁻⁴ as an adjunct to increase thyroid uptake of radio-iodine (¹³¹I) in the treatment of selected patients with nodular goitre (p.2165).

- Nielsen VE, *et al.* The effects of recombinant human thyrotropin, in normal subjects and patients with goitre. *Clin Endocrinol (Oxf)* 2004; **61**: 655-63.
- Duick DS, Baskin HJ. Significance of radioiodine uptake at 72 hours versus 24 hours after pretreatment with recombinant human thyrotropin for enhancement of radioiodine therapy in patients with symptomatic nontoxic or toxic multinodular goiter. *Endocr Pract* 2004; **10**: 253-60.
- Nielsen VE, *et al.* Recombinant human thyrotropin markedly changes the kinetics during therapy of patients with nodular goiter: an evaluation by a randomized double-blinded trial. *J Clin Endocrinol Metab* 2005; **90**: 79-83.
- Albino CC, *et al.* Recombinant human thyrotropin as adjuvant in the treatment of multinodular goiters with radioiodine. *J Clin Endocrinol Metab* 2005; **90**: 2775-80.

Malignant neoplasms of the thyroid. Patients with well-differentiated thyroid carcinoma (p.674) undergo surgery, with or without iodine-131 treatment. They then receive thyroid hormone therapy to suppress thyrotrophin (TSH), because most differentiated thyroid cancers express TSH receptors and grow in

response to thyrotrophin stimulation. Monitoring for tumour recurrence in subsequent years requires interruption of thyroid hormone treatment so that thyrotrophin levels rise, and stimulate the uptake of a subsequent dose of iodine-131 by any residual or recurrent tumour. However, this results in hypothyroidism, with associated symptoms that may be severe in some patients.¹

Studies^{2,3} have examined the use of thyrotrophin alfa as an alternative prelude to radio-iodine scanning, and found that it did stimulate radio-iodine uptake, although the sensitivity of scanning may depend on the technique used; thyrotrophin alfa might be considered a suitable alternative to thyroid hormone withdrawal. In patients with CNS or spinal metastases, or who have substantial disease in the thyroid bed, thyrotrophin alfa may cause tumour expansion with acute complications; it has been recommended¹ that prophylactic corticosteroid therapy should be considered in these cases.

Thyroid hormone withdrawal is also used in the treatment of differentiated thyroid cancer, to increase uptake of radio-iodine for thyroid remnant ablation and treatment of metastatic disease. The use of thyrotrophin alfa as an alternative adjunct is under investigation.⁴

- Basaria M, *et al.* The use of recombinant thyrotropin in the follow-up of patients with differentiated thyroid cancer. *Am J Med* 2002; **112**: 721-5.
- Ladenson PW, *et al.* Comparison of administration of recombinant human thyrotropin with withdrawal of thyroid hormone for radioactive iodine scanning in patients with thyroid carcinoma. *N Engl J Med* 1997; **337**: 888-96.
- Haugen BR, *et al.* A comparison of recombinant human thyrotropin and thyroid hormone withdrawal for the detection of thyroid remnant or cancer. *J Clin Endocrinol Metab* 1999; **84**: 3877-85.
- Robbins RJ, Robbins AK. Recombinant human thyrotropin and thyroid cancer management. *J Clin Endocrinol Metab* 2003; **88**: 1993-8.

Preparations

Proprietary Preparations (details are given in Part 3)

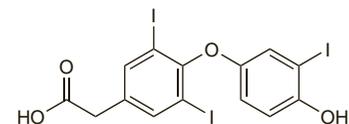
Austria: Thyrogen; **Belg.:** Thyrogen; **Braz.:** Thyrogen†; **Canada:** Thyrogen; **Cz.:** Thyrogen; **Denm.:** Thyrogen; **Fin.:** Thyrogen; **Fr.:** Thyrogen; **Ger.:** Thyrogen; **Gr.:** Thyrogen; **Hung.:** Thyrogen; **Israel:** Thyrogen; **Thyrotropin†; Ital.:** Thyrogen; **Neth.:** Thyrogen; **Norw.:** Thyrogen; **Pol.:** Thyrogen; **Port.:** Thyrogen; **Singapore:** Thyrogen; **Spain:** Thyrogen; **Swed.:** Thyrogen; **UK:** Thyrogen; **USA:** Thyrogen.

Tiratricol (rINN)

Tiratricolum; Tiratrikol; Tiratrikoli; Triac; Triiodothyroacetic Acid. [4-(4-Hydroxy-3-iodophenoxy)-3,5-diiodophenyl]acetic acid.

Тиратрикол

C₁₄H₉I₃O₄ = 621.9.
CAS — 51-24-1.
ATC — D11AX08; H03AA04.
ATC Vet — QD11AX08; QH03AA04.



NOTE. Tri-ac has also been used as a name for proprietary preparations containing other drugs.

Profile

Tiratricol, a metabolite of tri-iodothyronine, is reported to be less active than the thyroid hormones but is given orally to suppress the secretion of thyroid-stimulating hormone.

Obesity. Abnormal thyroid function tests, severe diarrhoea, fatigue, lethargy, and profound weight loss have occurred in patients taking dietary supplements containing tiratricol.^{1,2} The FDA has warned that tiratricol may cause heart attacks and strokes, and has advised consumers not to take these products.³

- Anonymous. Triac : a harmful product sold on the internet. *WHO Drug Inf* 2000; **14**: 30.
- Bauer BA, *et al.* Symptomatic hyperthyroidism in a patient taking the dietary supplement tiratricol. *Mayo Clin Proc* 2002; **77**: 587-90.
- FDA. FDA warns against consuming dietary supplements containing tiratricol. FDA Talk Paper T00-64, 21 Nov 2000. Available at: <http://www.fda.gov/bbs/topics/ANSWERS/ANS01057.html> (accessed 18/05/05)

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Dimagrin Triac†; Nulobes; Triacana; **Braz.:** Redulip†; Triac†; Trimag†; **Chile:** Triacana†; **Fr.:** Teatros; Triacana†.