Armour Thyroid (USP) and combined thyroxine/ tri-iodothyronine as Thyroid Hormone Replacement

A Statement from the British Thyroid Association Executive Committee

November 2007

Part 1. Use of Armour Thyroid

A. Armour Thyroid contains both thyroxine (T4) and tri-iodothyronine (T3) extracted from the thyroid gland of pigs. One grain, about 60 mg, of desiccated pig thyroid extract contains about 38mcg of T4 and 9mcg of T3, a ratio of around 4 to 1. The normal concentration of these hormones in the human thyroid is, however, at a ratio of 14 to 1. In other words, Armour thyroid extract contains excessive amounts of T3 relative to T4 when used to replace thyroid hormone in man. Moreover, as pig thyroid contains other substances apart from T4 and T3, Armour Thyroid is not a pure preparation of thyroid hormones. Historically, extracts of animal thyroid glands were the only way to treat thyroid underactivity, but since the 1950s pure synthetic thyroid hormones have been available in tablet form (thyroxine sodium [T4] and liothyronine [T3]).

B. The concentration of thyroid hormones in Armour Thyroid USP is regulated by the manufacturer to United States Food and Drug Administration (FDA) standards. Despite this, there have been significant problems with the stability of Armour Thyroid in recent years, prompting a massive recall of tablets.[1] Because of these stability problems with Armour Thyroid, there is potential for fluctuations in thyroid hormone levels in the blood of patients treated with Armour Thyroid. These fluctuations may be unpredictable and have adverse effects on patients' health.

C. There is no evidence to favour the prescription of Armour Thyroid in the treatment of hypothyroidism over the prescription of thyroxine sodium, as supplied in the United Kingdom. There has never been a direct comparison of these two treatments. The BTA committee cannot recommend a treatment with possible side-effects, when a safe and equally well-established treatment exists.

D. Armour Thyroid is not on the British National Formulary and is not a licensed therapy in the UK. Mr. G. Matthews, the Pharmaceutical Assessor of the Medicines and Health Care Products Regulatory Agency, in a letter sent to BTA dated 19 October 2005, has clarified that "The regulations on medicine allow doctors to prescribe an unlicensed medicine for a patient to meet such a special clinical need, on their own direct personal responsibility. Where these unlicensed medicines are not available in the UK they can be imported by appropriately licensed medicines wholesalers, for supply to a doctor or pharmacy, to meet these needs."

E. The cost of Armour Thyroid may be up to £20 per month, compared to an equivalent cost of £1 per month for thyroxine.

Part 2. Use of Combination Thyroxine/ Tri-iodothyronine (Liothyronine) Therapy

A. There is no currently available tablet preparation containing thyroxine and tri-iodothyronine (T4/T3) in a combination that adequately reproduces the relative quantities of these hormones produced by the human thyroid gland. Neither is there a preparation that produces a sustained release of thyroid hormones in a pattern similar to that from the human thyroid gland.

B. Having been disregarded as a therapeutic approach to the treatment of hypothyroidism since the 1970s, interest in combination thyroxine/tri-iodothyronine (T4/T3) therapy was re-ignited by a study of 31 patients published in 1999.[2] Although this study showed promising results, with improvement in quality of life, wellbeing and brain (psychometric) function with combination therapy, the majority of the patients in the study had been treated previously for thyroid cancer. The relatively high doses of thyroxine that formed the routine treatment for thyroid cancer (compared to a lesser replacement dose that would be normal in hypothyroidism) could have confounded the results of the study.

C. Since this initial study, there have been a further seven rigorously conducted ("randomised, double-blind, placebo-controlled") studies, encompassing more than 900 hypothyroid patients (summarised in refs. 3 & 4). None of the subsequent studies showed a beneficial effect of combined T4/T3 therapy on measures of wellbeing, health and mental functioning. Three of the seven studies show harmful or undesirable effects of the T4/T3 combination.

D. In three of the subsequent studies of combination treatment, the patients were asked which treatment they preferred, and in two of these 3 studies more patients preferred the combination T4/T3 therapy. There is no obvious explanation for these observations, and it may or may not be a reproducible effect.

E. The BTA keeps an open mind about whether using an appropriate formulation of T4/T3 combination tablet would, in the future, provide health and quality of life benefits in the treatment of hypothyroidism for a subgroup of patients. However, based on the current evidence from rigorous studies of large numbers of patients using the currently available formulations of synthetic thyroid hormones, combined T4/T3 cannot be recommended because of a lack of benefit and a small number of undesirable and harmful effects seen on combination treatment.

British Thyroid Association Executive Committee, November 2007

References

1. An FDA enforcement removed more than half a million bottles of Armour Thyroid from US pharmacies in 2005 due to unstable concentrations of thyroid hormone in the preparation. [www.fda.gov/bbs/topics/enforce/2005/ENF00899.html]

2. Bunevicius R, Kazanavicius G, Zalinkevicius R, Prange AJ Jr. Effects of thyroxine as compared with thyroxine plus triiodothyronine in patients with hypothyroidism. N Engl J Med. 1999; 340: 424-9.

3. Escobar-Morreale HF, Botella-Carretero JI, Escobar del Rey F, Morreale de Escobar G. Review: Treatment of hypothyroidism with combinations of levothyroxine plus liothyronine. J Clin Endocrinol Metab. 2005; 90: 4946-54.

4. Grozinsky-Glasberg S, Fraser A, Nahshoni E, Weizman A, Leibovici L. Thyroxine-triiodothyronine combination therapy versus thyroxine monotherapy for clinical hypothyroidism: meta-analysis of randomized controlled trials. J Clin Endocrinol Metab 2006; 91: 2592-9