

*A normal functioning thyroid gland releases both T4 (thyroxine) and T3 (triiodothyronine); the body converts T4 into T3 to meet its requirements.*

## **EVIDENCE FOR T3 USE IS WEAK**

Good evidence exists that treating with synthetic T4 alone is sufficient for maintaining good health in most people. Combined analysis of 11 studies in more than 1200 subjects concluded that there was no evidence to suggest that the combination of synthetic T4/T3\* is better than using only synthetic T4 in terms of quality of life or metabolic parameters. We know that a once daily synthetic T4 tablet can achieve similar physiological levels of T4 in the blood that would be measured in a person with a healthy thyroid.

*\*synthetic T3 (liothyronine)*

*\*synthetic T4 (levothyroxine)*

## **MONITORING T3 TREATMENT**

With synthetic T4 treatment we can use a simple blood test of the Thyroid Stimulating Hormone (TSH) level to adjust dose and monitor treatment. Using TSH to monitor synthetic T3 treatment may not be accurate. This is because T4 lasts several days in the body and the levels are very stable, whilst T3 lasts a day and the levels vary

throughout the day. Therefore, levels of TSH or T3 at one time point may not be a good reflection of thyroid hormone sufficiency.

Although we know severe hypothyroidism is associated with low body temperatures, using temperature monitoring to assess long term thyroid treatment has no scientific basis and is not an accepted practice.

## **T3 TREATMENT: SAFE OR UNSAFE?**

Unlike synthetic T4 treatment where there is plenty of data to demonstrate it is safe, there is only 1 observational study which suggests long term safety of combination T4 and T3 therapy. We know from people with overactive thyroids that too much thyroid hormone over long periods may cause serious complications. Oral synthetic T3 dosing can give peaks of T3 in the blood that are much higher than would be seen in a healthy patient or in a person treated with synthetic T4

The transient rise in serum T3 associated with synthetic T3 therapy may provoke abnormal heart rhythms in susceptible individuals and would be advised against in patients with heart disease. There are also concerns about too much thyroid replacement increasing the risk of osteoporosis (thin and fragile bones) in the long term.

Due to the risks of causing harm, better evidence is needed before routine synthetic T3 use can be routinely recommended.

## **GENETIC VARIABILITY DATA AND T3**

There is some evidence that a minority of individuals handle T4 to T3 hormone conversion differently due to genetic differences. In one study some of the patients who had a particular rare genetic variation reported symptom improvement on a combination of synthetic T3 and T4. The numbers involved were small and this finding is yet to be replicated in other trials. The study authors do not recommend using this genetic test (which is not available in routine clinical practice) to determine who should be treated with T3. This is because further studies are required to confirm this finding and the actual genetic cause.

## **NATURAL T3 - ARMOUR THYROID**

Armour thyroid (also known as natural desiccated thyroid, NDT) is a dried animal thyroid extract product that is not licensed in the UK. It contains higher amounts of T3 in relation to T4 than are normally present in humans. Furthermore, the proportions of T3 and T4 in each brand can vary. It is not licensed medication and has not undergone the same

safety testing that other medications have. It cannot be prescribed on the NHS.

The British Thyroid Association does not recommend its use as it may be unsafe in the long term.

## **WHAT DO THE THYROID ASSOCIATIONS SAY ABOUT TREATMENT WITH T3 – LIOETHYRONINE?**

The British Thyroid Association does not recommend T4/T3 routinely. If it is clear that all other options have been explored then a trial, supervised by endocrinologists, of T4/T3 may be considered after discussing the risks and benefits. However, an endocrinologist's clinical judgement may mean that this is not recommended.

The European Thyroid Association says that there is insufficient evidence to suggest T4/T3 combination is superior to T4 alone. It suggests that if other associated conditions have been ruled out, optimal biochemical control is achieved and there are persistent symptoms, then a trial of combination may be considered.

The American Thyroid Association says that T4 treatment alone should be used (as lack of evidence of benefit of combination and no long term data) and combination treatment should be considered only in a clinical trial setting.

## **COMPARATIVE COST**

Synthetic T3 as Liothyronine 10mcg twice daily costs approximately £1,700 per patient per year\*. Synthetic T4 as Levothyroxine 100mcg once daily costs approximately £22 per patient per year\*.

*\*Somerset NHS FT pharmacy data 2022*

## **SOMERSET SERVICES**

Some patients who experience persistent symptoms while taking T4 ask to trial taking combined T3/T4 therapy. Patients who have proven primary hypothyroidism (TSH >10 mu/l), have taken an appropriate dose of T4 for more than 1 year and in whom the symptoms are not explained by other medical conditions may be referred to be seen in a dedicated Endocrinology Thyroid clinic. Availability of these clinics is limited. When a patient is referred and their case accepted, they will be added to a waiting list. When seen, they will be assessed to see if a trial of T3/T4 is appropriate.

### ***Further reading***

<http://www.btf-thyroid.org/resources/news-archive/241-bta-statement-on-the-management-of-primary-hypothyroidism-2015>



## **Information for Patients**

### **Hypothyroidism**

## **The current evidence for T3 hormone replacement**