# Nottinghamshire Area Prescribing Committee Position Statement on Liothyronine (oral) for Hypothyroidism

Liothyronine (oral) is **not recommended** for prescribing in Nottinghamshire and is therefore classified **GREY**.

- Prescribing of liothyronine on the NHS in the Nottinghamshire area will only be supported in exceptional circumstances and only under recommendation from an NHS endocrinologist after a multidisciplinary discussion involving fellow consultants.
- Liothyronine (oral) is not supported by local NHS endocrinologists.
- NICE guidance: Do not routinely offer liothyronine for primary hypothyroidism, either alone or in combination with levothyroxine, because there is not enough evidence that it offers benefits over levothyroxine monotherapy, and its long-term adverse effects are uncertain.
- Liothyronine is included in the NHS England list of medicines that should not routinely be prescribed in primary care.
- Liothyronine costs vary according to the preparation used. At current costs, a 10 microgram twice daily dose costs between £553 and £3974 per patient per year. The equivalent daily dose of levothyroxine is 100 micrograms and costs the NHS approximately £10 per patient per year.
- There are potential risks from liothyronine therapy (on the bone-osteoporosis and the heart-arrhythmia).

## Background

Liothyronine (T3) is the active thyroid hormone and the majority is produced by peripheral conversion of levothyroxine (T4). Interest in the use of liothyronine in combination with levothyroxine has been in existence for many years, but there is currently no consistent evidence to suggest that combined therapy has advantages over therapy with levothyroxine alone. Levothyroxine alone is therefore the treatment of choice for hypothyroidism.

## Postulated rationale for liothyronine

Data suggest that 5–10% of levothyroxine-treated hypothyroid patients with normal serum TSH have persistent symptoms. There are several suggested explanations for this, but an inadequacy of levothyroxine to restore physiological T4 and T3 concentrations in serum and tissues and the existence of levothyroxine conversion disorders have been used as explanations in support of liothyronine treatment.

A study that investigated the effect of liothyronine treatment in patients with different genotypes for liothyronine conversion (deiodinase) enzymes has been quoted in support of the existence of a conversion disorder. A small number of patients with a certain genotype of the deiodinase 2 gene had worse psychological well-being at baseline and had greater improvements from liothyronine compared to placebo. No differences between genotypes in effects on thyroid function tests were seen. It is postulated that as deiodinase 2 is the only version of the enzyme able to convert T4 in the brain, certain genotypes may result in a poorer psychological response to T4 despite normalisation of thyroid function tests. **Genotype testing is not currently available in clinical practice and this study concludes that replication of the result is required *before changes in treatment approach can be recommend in routine practice.***

## Safety of liothyronine

The marked rise in serum free T3 associated with liothyronine therapy may provoke cardiac arrhythmias in susceptible individuals and it is contraindicated in patients with cardiovascular disease. There are also some concerns about an increased risk of osteoporosis.

**What to do with new requests for liothyronine and existing patients**

Advise that liothyronine is not recommended for prescribing within Nottinghamshire. Patients who have been seen privately should be referred back to the private service for private prescription of liothyronine or recommendation of an alternative treatment.

Prescribing of liothyronine on the NHS in the Nottinghamshire area will only be supported in exceptional circumstances and only under recommendation from an NHS endocrinologist after a multidisciplinary discussion involving fellow consultants. In these circumstances Primary Care prescribers may issue ongoing prescriptions. If in doubt, advice should be sought from a Senior Medicines Optimisation Pharmacist. It is expected that prescribing responsibility will remain with the specialist for at least the first 3-6 months of treatment and only transferred once there has been a formal assessment of the safety and benefit of treatment, evidenced by quality of life improvements and biochemical markers. Patients should remain under the care of an endocrinologist in line with RMOC guidance.

Costs of liothyronine preparations vary significantly. If liothyronine is to be prescribed on the NHS, the most cost-effective formulation should be chosen.

**Monitoring requirements**
Clinical and biochemical monitoring of treatment for potential side-effects should be undertaken. TSH levels should be maintained between 0.4-2.5mU/L with T3 and T4 in the normal range.

- TSH levels should be measured from blood tests taken **prior to the morning medication**.
- After dose stabilisation, annual monitoring is required unless there is a change in symptoms that may warrant the checking of TSH levels.
- Following a dose change a repeat test will be required at 6-8weeks.

For further information see RMOC / NHS England guidance for general practitioners and endocrinologists**.**
For patient information see Liothyronine information for patients.

**References:**
NICE Guidance (NG145): Thyroid disease: assessment and management, November 2019
Wiersinga WM et al. 2012 ETA Guidelines: The use of L-T4 + L-T3 in the treatment of hypothyroidism. Eur Thyroid J 2012;1:55-71
Panicker V *et al*. Common variation in the DI02 gene predicts baseline psychological well-being and response to combination thyroxine plus triiodothyronine therapy in hypothyroid patients. J Clin Endocrinol Metab, 2009; 94(5): 1623-1629.
NHS England: Items which should not routinely be prescribed in primary care: Guidance for CCGs, Version 2, June 2019.
RMOC Guidance – Prescribing of Liothyronine, V2.6 July 2019

Accessibility checked.