North Central London
Joint Formulary Committee

Oral liothyronine in Primary Hypothyroidism: Position Statement

New patients

Prescribers in primary care should not initiate liothyronine (T3) for adults, children and young people.

Consultant NHS Endocrinologists may offer liothyronine in rare situations for patients who meet national criteria. There is no obligation for endocrinologists to offer liothyronine owing to the limited evidence of benefit over levothyroxine (T4) monotherapy and uncertainty over long-term safety.

GPs should only take on prescribing of liothyronine where the treatment is recommended by a consultant NHS Endocrinologist, after a successful trial has been carried out. GPs should not take on prescribing for patients initiated on liothyronine in private clinics, abroad, or via other self-funded routes.

Existing patients

All patients prescribed liothyronine, either alone or in combination with levothyroxine, should be reviewed by a consultant NHS Endocrinologist with consideration given to switching to levothyroxine monotherapy where clinically appropriate.

This position statement does not apply to liothyronine as an adjuvant to radioactive iodine.

Background

- NICE NG145 'Thyroid disease: assessment and management' [1]:
  - Offer levothyroxine as first-line treatment for adults, children and young people for primary hypothyroidism.
  - 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.
- NHS England guidance: Prescribers in primary care should not initiate liothyronine for any new patient [2].
- RMOC guidance: A trial of liothyronine, usually in combination with levothyroxine, may be offered by a consultant NHS Endocrinologist in rare situations (see national criteria) [3].
- Many symptoms of hypothyroidism are the same as those of other conditions. For patients with persistent symptoms despite adequate replacement with levothyroxine (i.e. Thyroid Stimulating Hormone [TSH] level of 0.4-2.5mU/L) GPs should exclude where possible non-endocrine causes before referring to a consultant NHS Endocrinologist (see Table 1). Recommended tests include: HbA1c, FBC, Vitamin B12, Folate, Iron, U&E, Vitamin D & LFTs.

Patients initiating liothyronine for primary hypothyroidism

- There is no obligation for endocrinologists to offer liothyronine owing to the limited evidence of benefit over levothyroxine (T4) monotherapy and uncertainty over long-term safety [1,3].
- Any trial of liothyronine must adhere to national criteria and be supported by:
  - Endocrinology MDT
  - DTC/MMC secretariat or Trust's High-cost drugs panel (or equivalent)
  - Individual correspondence with the patient's GP
- Initial supply:
  - NHS Endocrinologist retains prescribing responsibility for 6 months, until the liothyronine dose is stable and a formal assessment of the safety and benefit of treatment has taken place
- Continuation assessment at 6 months by a consultant NHS Endocrinologist:
  - Improvement in quality of life (although it should be noted that the majority of randomised clinical trials have indicated a pronounced placebo effect), **and**
  - Maintain TSH of 0.4-2.5mU/L with the T4 in the normal range and ratio of dosages (in mcg) of daily T3:T4 not exceeding 1:20 to 1:13.
- GPs may continue prescribing after a positive assessment of benefit after 6 months
- GPs should not take on prescribing for patients initiated on liothyronine in private clinics, abroad, or via other self-funded routes. Consider offering patients the PrescQIPP Patient Information Leaflet to explain why the NHS is reducing prescribing of liothyronine.

National criteria for initiating a trial of liothyronine for primary hypothyroidism[3]

- Review by a consultant NHS Endocrinologist
- Eligibility for liothyronine in combination with levothyroxine:
  - Serum TSH within reference range with levothyroxine [TSH 0.4-1.5mU/L], **and**
  - Symptoms of hypothyroidism have a material impact upon normal day to day function, **and**
  - Alternative causes of symptoms have been excluded – see Table 1
- Eligibility for liothyronine monotherapy
  - Exceptional circumstances only e.g. specific levothyroxine medication intolerance confirmed by an NHS allergy service or cases of levothyroxine induced liver injury (extremely rare)
- Patient and clinician have discussed the uncertain benefits, likely risks of over-replacement (atrial fibrillation, osteoporosis and bone fractures) and lack of long-term safety data.

Table 1: Some possible causes of persistent symptoms in euthyroid patients on levothyroxine

Endocrine / autoimmune	Haematological	End organ damage	Nutritional	Metabolic	Drugs	Lifestyle	Other
Diabetes mellitus Adrenal insufficiency Hypopituitarism Coeliac disease Pernicious anaemia	Anaemia Multiple myeloma	Chronic liver disease Chronic kidney disease Congestive cardiac failure	Deficiency of any of the following: Vitamin B12 Folate Vitamin D Iron	Obesity Hypercalcaemia Electrolyte imbalance	Beta-blockers Statins Opiates	Stressful life events Poor sleep pattern Work-related exhaustion Alcohol excess	Obstructive sleep apnoea Viral and postviral syndromes Chronic fatigue syndrome Carbon monoxide poisoning Depression and anxiety Polymyalgia rheumatic Fibromyalgia

Patients already taking liothyronine for primary hypothyroidism

- Patients currently prescribed liothyronine monotherapy, or liothyronine in combination with levothyroxine should be reviewed by a consultant NHS Endocrinologist
- Consultant NHS Endocrinologist should:
  - identify when and why liothyronine was initiated
  - assess whether a trial titration to levothyroxine monotherapy is appropriate and either:
    - plan a trial titration to levothyroxine monotherapy where clinically appropriate, **or**
    - define the reason why a trial titration to levothyroxine monotherapy is inappropriate, confirm that liothyronine dose is appropriate and TSH is within acceptable ranges, and communicate this to the GP
- Patients who are currently obtaining supplies via private prescription or self-funding should not be offered NHS prescribing of liothyronine unless they are reviewed against national criteria by a consultant NHS Endocrinologist. Patients who have been seen privately retain the option of being referred back to the private service for private prescription

Trial titration to levothyroxine monotherapy

- The withdrawal of liothyronine should occur gradually in line with consultant NHS Endocrinologist recommendations, and may take many months to complete. Any withdrawal plan initiated in secondary care should be clearly communicated to the GP, along with any required monitoring.
- Conversion of patients from liothyronine to levothyroxine monotherapy will require a reduction in the dose of liothyronine and an increase in levothyroxine.
- There is no defined conversion factor however a reduction of dose of liothyronine by 20 micrograms daily will probably require an increase in dose of levothyroxine of 50 micrograms daily (e.g. levothyroxine 200 microgram each morning + liothyronine 10 microgram twice-daily → levothyroxine 250 microgram each morning)
- Once on levothyroxine monotherapy, patients will need to have adjustment in the dose as per standard practice by monitoring of the TSH on a 6 weekly basis (not more frequently as TSH will not have reached steady state) – see Table 2. After dose stabilisation, monitoring should only be required annually unless there is a change in symptoms that may warrant the checking of TSH levels
- Free T4 levels should also be measured where clinically appropriate.

Table 2: Actions to be taken in response to monitoring

TSH level	Action for GPs
More than 5 mU/L	Increase levothyroxine dose by 25 microgram
0.4 – 5.0 mU/L	No change required
Less than 0.4 mU/L	Seek specialist advice, likely resume at lower dose

Other recommendations

- Thyroid extracts (e.g. Armour thyroid, ERFA Thyroid), compounded thyroid hormones, iodine containing preparations, and dietary supplementation are not recommended. [3]
- Liothyronine in thyroid cancer, where it is used as an adjuvant to radioactive iodine treatment, should only be prescribed by specialists in secondary / tertiary care. Thyroid cancer patients who have completed their treatment usually need to take levothyroxine for life and should be managed in the same way as patients with hypothyroidism. [3]

References

1. NICE guideline NG145 – Thyroid disease: assessment and management (November 2019) link
2. NHS England – Items which should not routinely be prescribed in primary care: Guidance for CCGs (June 2019) link
3. Regional Medicines Optimisation Committee (RMOC) guidance – Prescribing of Liothyronine (July 2019) link

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