Liothyronine (including Armour® Thyroid and liothyronine combination products) Area Prescribing Committee Position Statement

The routine prescribing of liothyronine in primary care is <u>not supported</u> by Barnsley Area Prescribing Committee (APC). Liothyronine has a formulary red classification for new and existing patients.

In line with NHS England guidance:

- ***No <u>new patients</u> should be initiated on liothyronine in primary care. New patients should be initiated on liothyronine only in 'exceptional circumstances' by a consultant NHS endocrinologist and the specialist should continue the prescribing.***
- ***<u>Existing patients</u> currently prescribed liothyronine in primary care, either alone or in combination with levothyroxine, should be reviewed in liaison with a consultant NHS endocrinologist with consideration given to switching to levothyroxine monotherapy where clinically appropriate.***
    - ***On-going prescribing of liothyronine in existing patients, where there are 'exceptional circumstances' and on-going need for liothyronine has been confirmed by a consultant NHS endocrinologist, should remain with the secondary care specialist.***

Liothyronine is included in the NHS England guidance ***'Items which should not routinely be prescribed in Primary Care'*** *with some exceptions (see below)*.[1]

The price of liothyronine has risen significantly[1,] In Barnsley, primary care expenditure on liothyronine between October 2020 and September 2021 was approximately 16K.

The Medicines Management Team can support primary care prescribers to review patients on liothyronine.

Note that it is more cost effective to prescribe liothyronine capsules rather than tablets (see costs below)

<u>Exceptions and further recommendations</u>[1,2,3]

The British Thyroid Association (BTA) advise that a small proportion of patients treated with levothyroxine continue to suffer with symptoms despite adequate biochemical correction.

In these circumstances, where levothyroxine has failed and in line with BTA guidance, NHS England guidance advises that endocrinologists providing NHS services may recommend liothyronine for individual patients after a carefully audited trial of at least 3 months duration of liothyronine. The Barnsley Area Prescribing Committee has assigned liothyronine a red traffic light classification and the prescribing should remain with the specialist.

For new patients the RMOC recommends that strict criteria are applied to ensure that liothyronine is only prescribed in the situations where alternative treatments have found to be inadequate. In rare situations where patients experience continuing symptoms whilst on levothyroxine (that have a material impact upon normal day to day function), and other potential causes have been investigated and eliminated, RMOC advise that a 3 month trial with additional liothyronine may be appropriate. This is only to be initiated by a consultant NHS endocrinologist. Following this trial the consultant NHS endocrinologist will decide on the need for ongoing liothyronine. Many endocrinologists may not agree that a trial of levothyroxine /

liothyronine combination therapy is warranted in these circumstances and their clinical judgement is valid given the current understanding of the science and evidence of the treatments.

Liothyronine is used for patients with thyroid cancer, in preparation for radioiodine ablation, iodine scanning, or stimulated thyroglobulin test. In these situations it is appropriate for patients to obtain their prescriptions from the centre undertaking the treatment and not be routinely obtained from primary care prescribers.

Background and Rationale[1,2,4,5]

Liothyronine (sometimes known as L-T3) is used to treat hypothyroidism. It has a similar action to levothyroxine but is more rapidly metabolised and has a more rapid effect. It is sometimes used in combination with levothyroxine in products. Levothyroxine (L-T4) is a prodrug and is converted to liothyronine (L-T3) in the body.

Levothyroxine is the NHS thyroid hormone of choice as it is cost-effective, suitable for once daily dosing due to its long half-life and provides stable and physiological quantities of thyroid hormones for patients requiring replacement.

Liothyronine is not routinely recommended for prescribing as it has a much shorter half-life and steady-state levels cannot be maintained with once daily dosing.

The combination of levothyroxine and liothyronine, in both non-physiological and physiological proportions, has not consistently been shown to be more beneficial than levothyroxine alone with respect to cognitive function, social functioning and wellbeing. The variation in hormonal content and large amounts of liothyronine may lead to increased serum concentrations of L-T3 and subsequent thyrotoxic symptoms, such as palpitations and tremor.

Liothyronine is available as licensed 5microgram, 10microgram and 20microgram capsules and tablets (it is more cost effective to prescribe liothyronine capsules rather than tablets (see costs below)). Many other liothyronine-containing preparations (such as Armour® Thyroid) are unlicensed, therefore the safety and quality of these products cannot be assured.

The price (NHS Drug Tariff) of liothyronine has risen significantly and there is limited evidence for efficacy above levothyroxine.

The BTA, in their 2015 position statement, state "*There is no convincing evidence to support routine use of thyroid extracts, L-T3 monotherapy, compounded thyroid hormones, iodine containing preparations, dietary supplementation and over the counter preparations in the management of hypothyroidism".*

During the consultation period for the NHS England guidance evidence was received about a cohort of patients who require liothyronine in order to maintain health and wellbeing and the clinical working group felt it necessary to include some exceptions based on guidance from the BTA.

NICE NG 145 Thyroid: assessment and management states:

- Offer levothyroxine as first-line treatment for adults, children and young people with 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.
- Do not offer natural thyroid extract for primary hypothyroidism because there is not enough evidence that it offers benefits over levothyroxine, and its long-term adverse effects are uncertain.

Natural thyroid extract does not have a UK marketing authorisation so its safety is uncertain.

Deprescribing[1,3]

- Existing patients currently prescribed liothyronine in primary care, either alone or in combination with levothyroxine, should be reviewed in liaison with a consultant NHS endocrinologist in line with NHS England guidance with consideration given to switching to levothyroxine monotherapy where clinically appropriate. Prescriptions for individuals receiving liothyronine should continue until that review has taken place. In some cases a retrospective review of the basis for the original diagnosis of hypothyroidism may be necessary.
- The withdrawal or adjustment of liothyronine treatment should also only be undertaken by, or with the oversight of, an NHS consultant endocrinologist. Where GPs are involved in such treatment changes, this should be with NHS consultant endocrinologist support.
- If a previous trial titration has proved unsuccessful, the NHS consultant endocrinologist should decide whether a further review is warranted and inform the GP accordingly.
- The NHS consultant endocrinologist must specifically define the reason if any patient currently taking liothyronine should not undergo a trial titration to levothyroxine monotherapy, and this must be communicated to the GP and recorded on the patients' medical record.

Trial titration to levothyroxine: [3]

- There is no defined conversion factor, and conversion of patients from liothyronine to levothyroxine monotherapy will require a reduction in the dose of liothyronine and an increase in levothyroxine. A reduction of dose of liothyronine by 10 micrograms will probably require an increase in dose of levothyroxine of 50 micrograms. 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. Blood tests should not be undertaken more often than 6 weekly because the TSH will not have reached steady state until 6 weeks after any change. Free T4 / free T3 levels should also be measured where clinically appropriate.
- The withdrawal of liothyronine should occur gradually in line with NHS consultant 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.
- On-going prescribing of liothyronine in existing patients, where there are 'exceptional circumstances' and on-going need for liothyronine has been confirmed by a consultant NHS endocrinologist, should remain with the secondary care specialist.
- The following resources may be useful:
    - The BTA has produced a document for GPs, 'Switching your patient from Liothyronine (L-T3) to Levothyroxine (L-T4)? Answering GP's frequently asked questions': https://www.british-thyroid-association.org/sandbox/bta2016/faq_for_gps_.pdf
    - RMOC Guidance – Prescribing of liothyronine. June 2019. Available at: https://www.sps.nhs.uk/wp-content/uploads/2019/07/RMOC-Liothyronine-guidance-V2.6-final-1.pdf

Patient Information:

- An NHS patient information leaflet explaining the changes to liothyronine prescribing is available: https://www.prescqipp.info/resources/category/414-items-which-should-not-routinely-be-prescribed-in-primary-care-patient-leaflets

- BTA Frequently asked questions for patients: https://www.british-thyroid-association.org/sandbox/bta2016/faq_for_patients_.pdf

Costs

Price comparison for levothyroxine and liothyronine - Drug Tariff April 2022 and MIMS April 2022

Product	Cost per 28 tablets/capsules
Levothyroxine 12.5mcg tablet	£12.49
Levothyroxine 25mcg tablet	£0.95
Levothyroxine 50mcg tablet	£0.90
Levothyroxine 75mcg tablet	£2.58
Levothyroxine 100mcg tablet	£0.89
Liothyronine 5mcg capsule	£55.00
Liothyronine 10mcg capsule	£65.00
Liothyronine 20mcg capsule	£55.00
Liothyronine 5mcg tablet	£99.47
Liothyronine 10mcg tablet	£148.00
Liothyronine 20mcg tablet	£63.08

References

1. NHS England guidance 'Items which should not routinely be prescribed in Primary Care: Guidance for CCGs'. June 2019. Available at: https://www.england.nhs.uk/wp-content/uploads/2019/08/items-which-should-not-routinely-be-prescribed-in-primary-care-v2.1.pdf Accessed <12.10.21>
2. BTA guidelines. Available at: https://www.british-thyroid-association.org/current-bta-guidelines-and-statements Accessed <12.10.21>
3. RMOC Guidance – Prescribing of liothyronine. June 2019. Available at: https://www.sps.nhs.uk/wp-content/uploads/2019/07/RMOC-Liothyronine-guidance-V2.6-final-1.pdf Accessed <12.10.21>
4. PrescQIPP Bulletin 121: Switching liothyronine (L-T3) to levothyroxine (L-T4) in the management of primary hypothyroidism. February 2016. Available at: https://www.prescqipp.info/umbraco/surface/authorisedmediasurface/index?url=%2fmedia%2f1423%2fb121-liothyronine-drop-list-22.pdf Accessed <12.10.21>
5. NICE NG145: Thyroid assessment and management. November 2019. Available at: https://www.nice.org.uk/guidance/ng145/chapter/Update-information Accessed <12.10.21>

Further Information

SPS Avoid desiccated (natural) thyroid extract products for hypothyroidism. January 2022. Available at: Avoid desiccated (natural) thyroid extract products for hypothyroidism – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice

Development Process

This position statement has been subject to consultation and endorsement by the Endocrinologists in Barnsley and was ratified at the Area Prescribing Committee on 12th January 2022 (minor amendment: addition of liothyronine capsules June 2022).