DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Liothyronine in endocrinology position statement

For new patients*- liothyronine in combination with levothyroxine is **Do Not Prescribe** (DNP).

For existing patients**, following review of benefit by an NHS Endocrinologist specialist, liothyronine in combination with levothyroxine is **AMBER** **(see shared care).**

Liothyronine (L-T3) for monotherapy, , or in doses exceeding 60microgram per day is **RED**

This commissioning statement has been produced and endorsed by JAPC in response to an evidence review on the use of liothyronine, its cost effectiveness and affordability. This position statement is supported by local primary care clinicians and written in consultation with endocrinologists from provider organisations across Derbyshire.

Levothyroxine is the JAPC treatment of choice for hypothyroidism. It is cost-effective, suitable for once daily dosing, and provides stable and physiological quantities of a thyroid hormone for patients requiring replacement. All new patients requiring thyroid replacement will be initiated on **levothyroxine.**

For new patients* - liothyronine (L-T3) in combination with levothyroxine (L-T4) has been classified as **DNP** (Do Not Prescribe).

If there is an exceptional clinical need, such as difficulty in tolerating or absorbing levothyroxine, then a request to prescribe must be made via the IFR process and the request should be made by an NHS endocrinologist. Quality of life and other symptoms relating to patients lack well-being on levothyroxine monotherapy will not pass the test of exceptionality, and these patients should not be referred with the expectation that an IFR will be submitted. They can however still be referred to an endocrinologist for further evaluation of their symptoms to exclude other underlying medical conditions as well as optimisation of levothyroxine therapy.

For existing patients on liothyronine** - following NHS Endocrinologist specialist review to determine ongoing need, patients currently receiving liothyronine in combination with levothyroxine (L-T3 & L-T4) for ***hypothyroidism may continue treatment under a Derbyshire Shared Care Agreement - **AMBER** classification. Periodic reviews of ongoing need for liothyronine and potential dose reductions will be undertaken by the specialist.

Liothyronine when used as monotherapy, , or in doses that exceed 60microgram per day for any indication has been classified **RED**.

Exceptional acute use of liothyronine is permitted in oncology treatment and for diagnostic purposes in line with the British Thyroid cancer guidelines. (Classified as **RED**)

Desiccated thyroid products e.g. Armour thyroid/ERFA are classified as **DNP**. These are unlicensed products in the UK, derived from pig thyroid, and contain an excessive amount of L-T3 in relation to LT-4.

Patients who have been seen privately should be referred back to the private service if practicable, for continued private prescription of liothyronine or desiccated thyroid products (e.g. Armour thyroid/ERFA) or recommendation of an alternative treatment. Patients who wish to opt back into the NHS within Derby and Derbyshire integrated Care Board (ICB) commissioning geography will be treated as a new patient and assessed in the same patient pathway as an NHS patient.

*considered for treatment after publication of this statement (October 2019)

**commenced on treatment prior to the publication of this statement (October 2019)

***The symptoms of an underactive thyroid are not specific to the thyroid and may be due to many other conditions. If the TSH is within the reference range and dose adjustment has not helped, then the doctor should look for other causes of these symptoms. The list of possible alternative conditions is long but includes pernicious anaemia, coeliac disease, vitamin D deficiency, sleep apnoea, poor lifestyle and lack of sleep, depression, fibromyalgia, chronic fatigue syndrome and side-effects of medications.

Specialist review and managing existing patients being treated with liothyronine

The overall aim is to avoid over or under replacement with thyroid hormones. The suggested process is a gradual reduction of liothyronine while slowly introducing or increasing levothyroxine. This may help patients tolerate the change. 20-25microgram of liothyronine sodium is equivalent to approximately 100microgram of levothyroxine sodium.

Check TSH level before changing the patient's medications (every 4-6 weeks).

- If TSH is in the normal range introduce/increase levothyroxine by 25-50 microgram for every 10microgram of liothyronine reduction. Continue gradual reduction of liothyronine and increase of levothyroxine until patient is biochemically euthyroid and off Liothyronine.
- If starting TSH is <0.3mIU/L, reduce Liothyronine first by 10microgram every 4-6 weeks until TSH is in the normal range and then follow above advice.
- If TSH is >5.5mIU/L introduce/increase levothyroxine by 25microgram until TSH is in the normal range then follow above advice

Rationale

Cost effectiveness and affordability.

Levothyroxine (L-T4) is a pro-drug and is converted to liothyronine (L-T3) in the body. The price of liothyronine has increased significantly (in excess of 1000% since 2009) to the extent that JAPC now considers that on balance the £500k spend over 12 months for liothyronine, is no longer cost effective or affordable.

Desiccated thyroid compounds like Armour thyroid compared to levothyroxine are expensive for the NHS (a month of levothyroxine 100microgram costs less than £1, compared to around £40.00 for a month of natural desiccated thyroid of 120mg), with no obvious benefit.

Evidence and safety

There is currently insufficient evidence of clinical and cost effectiveness to support the routine use of liothyronine (either alone or in combination) for the treatment of hypothyroidism.

1. Liothyronine is considered an experimental approach by the European Thyroid Association in compliant levothyroxine-treated hypothyroid patients who have persistent complaints despite serum TSH values within the reference range. There is currently insufficient evidence to support the routine use of liothyronine outside a formal clinical trial.

2. The combination of levothyroxine and liothyronine, in both non-psychological and physiological proportions, has not consistently 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 liothyronine and subsequent thyrotoxic symptoms, such as palpitations and tremor.

3. Although some people report feeling better on liothyronine and levothyroxine, in "blinded" clinical trials, patients have not been able to tell the difference, except perhaps at high dose. It is harder to select, monitor and adjust the dose of liothyronine containing preparations than levothyroxine, and it is likely therefore that using liothyronine and levothyroxine will increase the risk of stroke and osteoporosis from slight over treatment over many years.

4. Liothyronine has a much shorter half-life and steady-state levels cannot be maintained with once daily dosing.

5. Unlicensed products e.g. Armour Thyroid, ERFA are not subject to the same assurances of quality, safety and efficacy as licensed medicines and should not be prescribed where a licensed product like levothyroxine is available.

Further resources

British thyroid association http://www.british-thyroid-association.org/current-bta-guidelines-

Switching from liothyronine (LT-3) to levothyroxine (LT-4)

- Frequently Asked Questions for GP's
- Frequently Asked Questions for patients
- Information for Endocrinologists

SPS Avoid desiccated (natural) thyroid extract products for hypothyroidism

NHSE Liothyronine – advice for prescribers

Reference

1. Okosiemi, O, Gilbert J, Abraham P et al. Management of primary hypothyroidism: statement by the British Thyroid Association Executive Committee. Clinical Endocrinology 2015;0:1-10.
2. Wiersinga W, Duntas L, Fadeyev V, Nygaard B, Vanderpump M. 2012 ETA Guidelines: The Use of L-T4 + L-T3 in the Treatment of Hypothyroidism. Eur Thyroid J 2012;1:55–7. DOI: 10.1159/000339444. Accessed on 14/6/2017
3. Presqipp bulletin 121 Switching liothyronine (L-T3) to levothyroxine (L-T4) in the management of primary hypothyroidism. December 2015
4. British Thyroid Association. Q&As to accompany the 2015 BTA Statement on the Management of Hypothyroidism. December 2015
5. British Thyroid Association. Information for members on the prescribing of liothyronine. December 2016
6. Use of liothyronine (T3) in hypothyroidism: Joint British Thyroid Association/Society for endocrinology consensus statement

Document control	Date
Addition of word endocrinology to document title	Dec 2024
Removal of RED TLC status for prescribing in resistant depression	Dec 2024
Update of resources	Dec 2024