Liothyronine / Natural Desiccated Thyroid Extract (NDT) (Armour Thyroid, Nature Thyroid, WP Thyroid, ERFA Thyroid and other brands) – Questions and answers for primary care colleagues in Sheffield CCG

Q1. What are the differences between levothyroxine (L-T4), liothyronine (L-T3) and desiccated thyroid extract?

A - Levothyroxine (L-T4) is a prodrug and is converted to liothyronine (L-T3) in the body. Desiccated thyroid extract is of animal origin (porcine or less commonly bovine) containing both levothyroxine and liothyronine in a non-physiological ratio. The T4:T3 ratio in desiccated thyroid extract is 4:1, compared to the normal physiological ratio of 14:1.

Before the 1970s, synthetic combinations of levothyroxine and liothyronine or desiccated animal thyroid extract containing varying amounts of thyroid hormones were used, but these have now been superseded by levothyroxine monotherapy.

Q2. Why is levothyroxine preferred?

A - Levothyroxine is the 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 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.

Unlike levothyroxine, there is no long term safety data for liothyronine use either alone or in combination with levothyroxine.

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

Q3. Should patients currently taking liothyronine be switched to levothyroxine?

A - Patients currently prescribed liothyronine alone or in combination with levothyroxine, including desiccated thyroid extract should be reviewed by GPs with a view to switching them to levothyroxine monotherapy. GPs should have an open and frank discussion with patients in light of: the significant increase in the cost of liothyronine; recent guidance from NHSE (Items which should not routinely be prescribed in primary care: Guidance for CCGs - ref 1); the addition of liothyronine to the STOP list and the black section of the traffic light drug list in Sheffield (if being used for long term replacement therapy, see Q4 if being used for thyroid cancer). The discussion should address patients' expectations to minimise anxiety and potential concerns.

If the patient is willing to consider changing to levothyroxine, then depending on regime / preparation follow the options below:

If taking liothyronine in combination with levothyroxine **either**:

- Switch from liothyronine to levothyroxine gradually aiming to avoid under or over-replacement with thyroid hormones. The final L-T4 requirement is likely to be around 1.6microgram/kg. Any information about previous L-T4 dosage that achieved a serum TSH

within the reference range will be a useful guide that predicts the individual requirement. Most patients will be taking liothyronine 10micrograms once or twice daily in combination with levothyroxine. Start by replacing 10micrograms of liothyronine initially with 25 micrograms of levothyroxine and check thyroid function tests in 4 – 6 weeks. Adjust the dose of thyroxine according to the serum TSH concentration. Once serum TSH is normalised continue monotherapy or, if on a twice daily regimen, effect further withdrawal of second liothyronine dose and further adjust levothyroxine dose if required. The goal of treatment is restoration of well-being whilst maintaining a serum TSH within normal reference range. In practice, this is likely to mean a serum TSH below 2 mIU/L.

or

- *Seek advice in writing from the endocrine department at RHH, or via the advice and guidance service once this is operational in the future (Details to follow)

or

- *Refer to endocrinologist for a face to face review, making it clear to patients that the referral is for review of treatment and not necessarily an appointment to stop treatment, so that expectations are managed.

*Recommended options for patients on more complex regimens.

If taking liothyronine monotherapy either:

- Seek advice in writing from the endocrine department at RHH, or via the advice and guidance service once this is operational in the future (Details to follow)

or

- Refer to endocrinologist for a face to face review, making it clear to patients that the referral is for review of treatment and not necessarily an appointment to stop treatment, so that expectations are managed.

If the patient is not willing to change to levothyroxine after discussion with GP/ endocrinologist then GPs can continue to prescribe liothyronine as before, however it is recommended the discussion is documented and reviewed periodically.

If patient is taking desiccated thyroid extract:
Desiccated thyroid extract is on the black section of the traffic light drug list in Sheffield. It is unlicensed and there is a lack of evidence supporting effectiveness (ref 3) and so should not be prescribed on the NHS. Ongoing supplies can only be ensured through private prescriptions for which the patient will need referral to a private endocrinologist. If the patient wishes to be switched to levothyroxine or levothyroxine / liothyronine combination then a referral should be made to an NHS endocrinologist, however expectations should be managed as patient may not be eligible for IFR funding for liothyronine.

Q4. Should patients with thyroid cancer also be switched to levothyroxine?
A - If liothyronine has been prescribed for thyroid cancer patients in preparation for radioiodine ablation, iodine scanning or a stimulated thyroglobulin test, it is strongly recommended that liothyronine should not be discontinued or converted to levothyroxine. The prescription of liothyronine in these cases should be done by the centre undertaking treatment. Any long term prescribing of liothyronine in thyroid cancer patients should be undertaken by the cancer centre responsible for their care.

Q5. Are there any particular types of patients which merit extra caution when switching from liothyronine to levothyroxine?
A- In patients over 60 years, or those of any age with known ischaemic heart disease, additional care should be taken to avoid over-replacement.

Q6. What should GPs do in case of a new patient request for liothyronine?
A- Liothyronine is in the black section of the traffic light drug list in Sheffield and cannot be initiated in new patients. 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 of 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.

Q7. What should GPs do for patients who have been started on liothyronine privately?
A - See Question 3 and 6 and also the 'NHS Sheffield CCG Medicines Code' 5.6.1

Authors

Dr Fahad Arshad, Specialist Registrar in Endocrinology, Sheffield Teaching Hospitals NHS Foundation Trust
Dr Amit Allahabadia, Consultant Endocrinologist, Sheffield Teaching Hospitals NHS Foundation Trust
Heidi Taylor, Clinical Effectiveness Pharmacist, NHS Sheffield CCG.

Approved APG - September 2018 Minor amendment November 2018

Review – 3 years

References

1 -Items which should not routinely be prescribed in primary care: Guidance for CCGs https://www.england.nhs.uk/wp-content/uploads/2017/11/items-which-should-not-be-routinely-precscribed-in-pc-ccg-guidance.pdf

2 - Current BTA guideline - http://www.british-thyroid-association.org/current-bta-guidelines-