NHS
Devon
Clinical Commissioning Group

Protocol to initiate new patients on Liothyronine

NHS Devon Clinical Commissioning Group

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All policies are held centrally by Governance: d-ccg.governance@nhs.net		

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0.1	06/12/17	First draft
0.2	22/03/18	Amendments following 1st consultation with endocrinologists
0.3	23/05/18	Appendix – referral details added plus further minor amendments
0.4	13/06/18	Comments following endocrinologists meeting
0.5	05/07/18	Comments from LMC clinical secretary
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0.8	02/05/19	Changes following e-FIG consultation
0.9	07/05/19	Re-formatted
1.0	15/05/19	Re-formatted following approval by Business Commissioning Meeting

Equality, diversity and inclusion statement

NHS Devon CCG is committed to the promotion of equal opportunities, addressing health inequalities and fostering of good relations between people protected under the terms of the Equality Act 2010, the Health and Social Care Act 2012 and Human Rights legislation. We are equally committed to the elimination of unlawful discrimination, harassment and victimisation. To demonstrate this commitment, we develop, promote and maintain policies, strategies and operating procedures. Every effort is made to ensure that patients, employees, contractors or visitors do not experience discrimination; either directly or indirectly, because of their vulnerability; disadvantage; age; disability; gender reassignment; marriage and civil partnership; pregnancy and maternity; race; religion and belief; sex (gender) or sexual orientation.

All staff must comply with this policy. Compliance must reflect our organisational commitment to and policy on, equality, diversity and inclusion. In addition, each manager and member of staff involved in implementing this policy must give due regard to the needs of those protected under law.

If you, or any other groups, believe you are discriminated against under the terms of the Equality Act, the Health and Social Care Act 2012 or Human Rights legislation by anything contained in this document; or you need this document in an alternative format, for example, large print, Braille, Easy read or other languages; please contact our Patient Advice and Complaints Team (PACT):

Tel: 0300 123 1672
Email: pals.devon@nhs.net,
Post: Patient Advice and Complaints Team,
FREEPOST EX184,
County Hall,
Topsham Road
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1. Overview

Liothyronine (T3) is a very expensive treatment used in a small number of hypothyroid patients due to sub-optimal response to the usual treatment, levothyroxine (T4). The evidence to support use of liothyronine is very limited and is insufficient to justify the high financial cost currently incurred.

NHS England has advised CCGs (30th November 2017) that:

- There should be no new initiations of liothyronine in primary care
- Individuals currently prescribed liothyronine should be reviewed by a consultant NHS endocrinologist with consideration given to switching to levothyroxine where clinically appropriate, **but that**:
- The British Thyroid Association (BTA) advice is 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, endocrinologists providing NHS services may recommend liothyronine for individual patients after a carefully audited trial of at least 3 months duration of liothyronine.

https://www.england.nhs.uk/publication/items-which-should-not-be-routinely-prescribed-in-primary-care-guidance-for-ccgs/

Further guidance is available from the Regional Medicines Optimisation Committee (RMOC) https://www.sps.nhs.uk/articles/rmoc-guidance-prescribing-of-liothyronine/ The aim of this guidance is to inform CCGs and Area Prescribing Committees in local decision making, and support a consistent approach for the exceptional circumstances in which patients have an on-going need for liothyronine.

Consultation has taken place between the Devon CCGs, specialist endocrinologists and primary care to agree the basis on which the existing patients will be reviewed in accordance with the NHSE / RMOC guidance. This protocol describes that process and the responsibilities of the clinicians involved in caring for these patients. There is a separate but closely aligned protocol for initiating new patients on liothyronine. The Devon Formulary section on thyroid hormones are available at:

South and West:
https://southwest.devonformularyguidance.nhs.uk/formulary/chapters/6.-endocrine/6.2-thyroid-and-antithyroid-drugs/6-2-1-thyroid-hormones-1
North and East:
https://northeast.devonformularyguidance.nhs.uk/formulary/chapters/6.-endocrine/6.2-thyroid/6-2-1-thyroid-hormones

2. Primary Care Responsibilities:

2.1 There should be **no new initiations in primary care**

2.2 If considering a new initiation of liothyronine before referrals to endocrinology, ensure that levothyroxine prescribing is optimal. Consider:

- A thorough evaluation of other potentially modifiable conditions (see **appendix 1**). Any relevant conditions should be corrected where possible before changing thyroid treatment.
- Repeating Thyroid Function Tests (TFTs) 2-3 months after starting levothyroxine
- If TFTs are not within the normal range adjust the dose of levothyroxine and allow 2-3 months for symptoms to stabilise
- Due to its long half-life, levothyroxine 25 microgram tablets may be given on alternate days for fine adjustment of dosage
- If alternate day 25 microgram dosing is not successful, try 12.5 microgram tablets daily for fine control if necessary (these are more expensive than the other strengths of levothyroxine but much cheaper than liothyronine)
- Branded levothyroxine (Eltroxin®) may be considered as only marginally more expensive than generic. Although the BTA state “For the vast majority of patients on levothyroxine, brand or named supplier prescribing is not considered necessary (2/+00)”, the MHRA has stated “Rarely, patients may require a specific brand of levothyroxine to be prescribed due to intolerance of generic preparations.”

2.3 Patients that genuinely do not have symptom improvement on levothyroxine, where the symptoms are felt to be compatible with the thyroid and have TFTs in the normal range can be considered for referral to the Endocrinology Clinic for assessment (see **appendix 2** for referral details).

2.4 GPs should not refer patients to endocrinology unless they are prepared to continue prescribing of liothyronine should it be initiated in and recommended to continue by secondary care as per the process described below.

2.5 For patients initiated by secondary care and continued as per the specialist advice below: refer to the review section of the existing patients’ protocol.

2.6 Strict control of the issue of liothyronine tablets will be necessary. There should be no early or extra prescriptions provided (apart from appropriate quantities for holidays)

3. Secondary Care Responsibilities

3.1 Assessment by endocrinology to confirm a thorough evaluation of other potentially modifiable conditions has been done (see **appendix 1**). Any relevant conditions should be corrected where possible before changing thyroid treatment.

3.2 Before considering liothyronine ensure that levothyroxine prescribing is optimal as in 2.2 above

3.3 Additionally, endocrinologists may wish to up titrate levothyroxine even at expense of TSH being below reference range (but not < 0.1mU/L, as this carries a risk of serious cardiac effects, strokes and osteoporosis).

3.4 If symptoms persist despite all the above, clearly document the main symptoms that the patient finds troublesome. There should be an open and balanced discussion of the uncertain benefits, likely risks of over-replacement and lack of long-term safety data for liothyronine. Provide written information and if the patient still wishes to go ahead offer a trial of 2 months combination levothyroxine / liothyronine treatment (two packs of 28 x 20 micrograms liothyronine) initiated by secondary care:

- The licensed product of liothyronine 20microgram tablets must be used. Lower strength tablets / capsules and all liquids are unlicensed specials. These can be even more expensive than the licensed tablets, are of unknown quality / stability and prescribers are not supported by a product licence.
- Liothyronine 20 microgram tablets are scored but the SPC does not allow the breaking of tablets for lower doses The SPC recommends the following method to take / administer doses below 20 micrograms:

    - the tablet should be allowed to dissolve/disperse in 20 mL of water for 10 minutes, in a small measuring cup.

    - The patient should gently swirl the solution occasionally to aid the dissolution/dispersion. The patient should then swirl the solution for a few seconds prior to using a suitable oral syringe to withdraw the amount of liquid corresponding to the dose prescribed (5mL for a 5mcg dose; 10 mL for a 10mcg dose).
    - The patient can then squirt the liquid directly into their mouth from the suitable oral syringe by gently pressing the plunger.

    - Any remaining liquid should be discarded.

- The usual aim should be to re-establish the patient on combined treatment with a levothyroxine: liothyronine dose ratio of 10:1 or higher, with a maximum dose of 10micrograms daily liothyronine, taken either once daily or in two divided doses.

- Initial monitoring of TFTs should occur after 6-8 weeks and after each medication change to ensure TSH does not become suppressed. There should be a formal assessment as close to 3 months as possible to ensure there has been an improvement in the agreed symptoms which were important to the patient (and thought to be relevant to the thyroid).

- If there is no evidence of ongoing clinical benefit, then combination levothyroxine and liothyronine is to be discontinued and converted back to levothyroxine monotherapy.

- The first prescription for liothyronine should be for two packs of 28 x 20microgram tablets at a dose of 10 micrograms daily i.e. 56 days' supply. Note: the budget for this prescribing to be transferred from primary care. After the formal assessment if prescribing is to continue it will be provided by primary care.

- Secondary care to ensure full liaison with primary care regarding the outcome of the trial of levothyroxine/liothyronine and whether prescribing is to continue.

3.5 Levothyroxine / liothyronine combination therapy or liothyronine monotherapy is contraindicated in pregnancy

3.6 Once stable, offer discharge back to primary care (if GP in agreement) with phone / email advice about dosing if helpful.

Appendix 1

Some possible causes of persistent symptoms in euthyroid patients on levothyroxine to be considered by primary care prior to referral to secondary care

Ref: Management of primary hypothyroidism: statement by the British Thyroid Association Executive Committee, Clinical Endocrinology 2015.

Endocrine/ auto-immune

Diabetes mellitus	Adrenal insufficiency	Hypopituitarism	Coeliac disease
Pernicious anaemia			

Haematological

Anaemia	Multiple myeloma

End-organ damage

Chronic kidney disease	Chronic liver disease	Congestive cardiac failure

Nutritional

Vitamin B12 deficiency	Folate deficiency	Vitamin D deficiency
Iron deficiency		

Metabolic

Obesity	Hypercalcaemia	Electrolyte imbalance

Drugs

Beta-blockers	Statins	Opiates

Lifestyle

Stressful life events	Poor sleep pattern	Work-related exhaustion
Alcohol excess		

Others

Obstructive sleep apnoea	Viral and post viral syndromes	Chronic fatigue syndrome
Carbon monoxide poisoning	Depression and anxiety	Polymyalgia rheumatica
Fibromyalgia		

Appendix 2

Patient not responding / tolerating levothyroxine:

Referral details

- Initial diagnostic TFTs (**was TSH ever raised?** - **this is crucially important so please prioritise over other information**)
- Current dose levothyroxine
- Start date
- Started by whom
- Reasons for starting
- Relevant endocrinological history prior to and after starting levothyroxine including relevant monitoring and TSH results
- Current ongoing problem
- Relevant past medical history
- Current other medication (any relevant past medication history)