

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

LIOTHYRONINE FOR THE TREATMENT OF HYPOTHYROIDISM

RED – NOT RECOMMENDED FOR PRESCRIBING IN PRIMARY CARE (NEW PATIENTS)

Name:	Indication	Decision last revised	Decision Status	NICE / SMC/ NHSE Guidance
Liothyronine	Hypothyroidism	March 2018	Final	NICE and SMC - No Guidance NHSE – November 2017

HMMC Recommendation (In line with East of England Priorities Advisory Committee recommendations):

New Patients:

New patient prescribing should remain with the hospital specialist

Existing patients

Patients who are already receiving liothyronine on prescription from their GP, prescribing to remain in primary care

Prescribing guidance will be developed jointly by primary and secondary care to support GPs to review and switch existing liothyronine patients to levothyroxine where clinically appropriate, with support from a consultant NHS endocrinologist where necessary.

East Of England Priorities Advisory Committee recommendations

- Levothyroxine monotherapy is the treatment of choice for hypothyroidism. There is no consistent evidence to support the routine use of liothyronine in the management of hypothyroidism, either alone or in combination with levothyroxine.
- Liothyronine for treatment of hypothyroidism is not recommended for routine funding unless one of the following criteria applies:
 - Post thyroidectomy thyroid cancer patients. Patients who need to receive radioactive iodine treatment (Radioiodine Remnant Ablation RRA) after their surgery will initially be started on liothyronine due to its shorter half-life and therefore faster onset of action than levothyroxine. These patients will remain on liothyronine until the oncologist is confident that they will not need any more radioactive iodine at which point they are switched over to levothyroxine. Prescribing in these circumstances must remain with the secondary care specialist and GPs should not accept prescribing responsibility for these patients.
 - In rare cases of levothyroxine induced liver injury, long term liothyronine prescribing may be supported.
- Initiation and prescribing of liothyronine for patients on levothyroxine who continue to suffer with symptoms despite adequate biochemical correction should remain in secondary care under the supervision of an accredited endocrinologist.
- Funding of unlicensed medicines e.g. Armour Thyroid for the treatment of hypothyroidism is not supported.
- Prescribers in primary care should not initiate or accept clinical responsibility for on-going prescribing of liothyronine for any new patient, including patients who are currently self-funding and obtaining supplies via private prescription or previously prescribed by a secondary care consultant, unless the criteria stated above are met and they have agreed to accept clinical responsibility for prescribing.
- CCGs should give consideration to providing guidance for GPs to switch existing patients to levothyroxine where clinically appropriate, with support from a consultant NHS endocrinologist where necessary or agree arrangements for appropriate review by a consultant NHS endocrinologist
- These recommendations will be reviewed in the light of new evidence of clinical and cost effectiveness.

Mode of Action

- 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 (L-T3) 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. In primary care L-T3 should not be prescribed alone apart from in rare cases of levothyroxine induced liver injury.

Unlicensed products

Use of unlicensed strengths of L-T3 and dried thyroid hormone extracts, such as **Armour® Thyroid, is NOT recommended.**

Armour® thyroid is desiccated thyroid extract derived from porcine thyroid gland. One grain contains 38mcg L-T4 and 9mcg L-T3 per 65mg of the labelled amount of thyroid. Prescribers and patients should be aware that the amount of thyroid hormone in the thyroid gland can vary from animal to animal and between batches of product so a consistent effect cannot be guaranteed with desiccated thyroid extract products. Armour® thyroid is not licensed in the UK.

Unlicensed indications

Use of liothyronine for unlicensed indications is **NOT recommended**. There is insufficient evidence for use of liothyronine for unlicensed indications such as for use as an adjunctive treatment to tricyclic antidepressants in patients with refractory severe depression.

Assessment against Ethical Framework

Evidence of Clinical Effectiveness

- No consistent evidence to support the routine use of L-T3 in the management of hypothyroidism, either alone or in combination with L-T4. Data from several, small and methodologically limited trials have failed to clearly demonstrate superiority of combination L-T3/L-T4 treatment over L-T4 monotherapy.
- Clinical practice guidelines, worldwide, do not recommend and do not support the routine use of combination L-T3 and L-T4 therapy for hypothyroidism
- There is a lack of evidence to support long term monotherapy with L-T3.
- A systematic review of nine randomized trials confirmed that only one study (Bunevicius et al) has reported beneficial effects of combination with L-T4 – L-T3 therapy on mood, quality of life, and psychometric performance when compared to L-T4 therapy alone and another systematic review by Grozinsky-Glasberg et al, concludes that L-T4 monotherapy is the treatment of choice for clinical hypothyroidism.
- 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

Safety:

- L-T3 intestinal absorption can give rise to unusually high post absorption peaks leading to tachycardia and consequently there may be an increased risk of cardiac complications.
- The dosage needed to obtain euthyroidism with L-T3 is more difficult to evaluate, owing to unpredictable fluctuations in serum L-T3 concentration.

Cost of treatment and cost-effectiveness

- No studies on cost-effectiveness identified.
- NHS England (NHSE) “Items which should not routinely be prescribed in primary care” lists LT-3 as a drug of low priority as it is of high cost and with limited evidence and where the vast majority of patients can be controlled on much cheaper LT-4. However, NHSE did acknowledge that a small proportion of patients treated with L-T4 continue to suffer symptoms despite adequate biochemical correction. In these circumstances where L-T4 has failed and in line with British Thyroid Association guidance endocrinologists providing NHS services may recommend L-T3 after a carefully audited trial of at-least 3 months duration of L-T3
- The BNF states that 20–25 micrograms of L-T3 is equivalent to 100 micrograms of L-T4.

Price comparison table – Drug tariff March 2018

Product	Cost per 28 tablets
Levothyroxine 100 microgram tablets	£1.09
Product	Cost per 28 tablets
Liothyronine 20 microgram tablets	£249.98
Liothyronine 5 microgram tablets (special without a UK license)	£83.61 average cost for 28 (ePACT data HVCCG)
Armour thyroid (special without a UK license available in various strengths)	£56.42 average cost for 28 (ePACT data HVCCG)

The needs of the population

The needs of the population appear to be low as there is an alternative treatment (L-T4) which is lower cost. It is however acknowledged that there may be a sub-set of exceptional cases that may benefit from a trial of combination therapy, following inadequate control on L-T4.

The needs of the community

The needs of the community are small as L-T3 is not required in the vast majority of patients with hypothyroidism. The impact on the health economy appears to be high as L-T3 has a high cost and its cost is higher than other alternative pharmacological therapies.

Policy Drivers

NHS England guidance in November 2017 lists L-T3 as an “item which should not be routinely prescribed in primary care.” Clinical practice guidelines, worldwide, do not recommend and do not support the routine use of combination L-T4 and L-T3 therapy for hypothyroidism, including NICE Clinical Knowledge Summary, British Thyroid Association, American Thyroid Association and European Thyroid Association guidance

Equity

No impact anticipated

Implementability

Widespread prescribing in primary and secondary care. Review of existing patients in primary care will require support. Prescribing guidance documentation will be developed with the support of secondary care.

References

- Management of primary hypothyroidism: statement by the British Thyroid Association Executive Committee. Clinical Endocrinology (2016) 84, 799–808 <http://onlinelibrary.wiley.com/doi/10.1111/cen.12824/pdf>
- The Diagnosis and Management of Primary Hypothyroidism, Royal College of Physicians 2011 [Link](#)
- What clinical evidence is there to support the use of “Armour thyroid” or other desiccated thyroid extract products? UKMI Medicines Q&A 56.7 February 2016 [Link](#)
- Prescripp bulletin 121 February 2016 Switching liothyronine (L-T3) to levothyroxine (L-T4) in the management of primary hypothyroidism [Link](#)
- NHS England: Items which should not routinely be prescribed in primary care. Available at: <https://www.england.nhs.uk/wp-content/uploads/2017/11/items-which-should-not-be-routinely-prescribed-in-pc-ccg-guidance.pdf>.
- The East of England Priorities Advisory Committee – Commissioning recommendations for Liothyronine (all indications).