PrescQIPP Community Interest Company

Switching liothyronine (L-T3) to levothyroxine (L-T4) in the management of primary hypothyroidism

This is one of a number of bulletins providing further information on medicines contained in the PrescQIPP DROP-List (Drugs to Review for Optimised Prescribing). This bulletin focuses on liothyronine and provides the rationale for new patients to be commenced on levothyroxine and for current patients to be considered for a switch to levothyroxine. Information on liothyronine adverse effects, options for dose conversion in support of the switch and potential switch savings are provided. Further bulletins, including the DROP-List, are available on the PrescQIPP website www.prescqipp.info[1]

Recommendations

- Ensure that prescribing of thyroid hormones is in line with British Thyroid Association (BTA) guidance.[2] http://www.british-thyroid-association.org/news/BTA_Hypothyroidism_Statement.pdf
- Commence new patients requiring thyroid replacement on levothyroxine.
- Review all patients taking liothyronine (alone or in combination with levothyroxine) for suitability for switching to levothyroxine. Switch all suitable patients to levothyroxine. For patients under the care of a relevant specialist, involve them in the decision to switch to levothyroxine.
- It may be necessary in some cases to establish patient is genuinely hypothyroid before swapping (historically confirmed on biochemistry in accredited NHS lab or if not stop treatment and show thyroid stimulating hormone (TSH) rise). In these cases, start with standard dose of levothyroxine and titrate.
- CCG Medicines Management Teams should liaise with local endocrinologists to ensure that prescribing is consistent across the interface between primary and secondary care.
- As with all switches, these should be tailored to the individual patient.

Background

The PrescQIPP DROP-List is an accumulation of medicines that are regarded as low priority, poor value for money or medicines for which there are safer alternatives. Medicines that could be considered for self care with the support of the community pharmacist are also included on the DROP-List. Liothyronine features on the DROP-List as an item which is poor value for money and has limited clinical value.

Nationally over £20.8 million was spent on liothyronine over the course of a year (ePACT May to July 2015). Switching to levothyroxine could release significant savings nationally. As with all switches, individual patient circumstances need to be borne in mind, however, with tight switching criteria, assistance from practice nurses, support from your local CCG prescribing teams and the experiences of CCGs/GPs that have already undertaken this work, it is hoped that GPs will participate in realising the cost savings.

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Rationale for switching to levothyroxine

- Levothyroxine (L-T4) is a prodrug and is converted to liothyronine (L-T3) in the body.[3] Prior to the 1970s, synthetic combinations of levothyroxine and liothyronine or desiccated animal thyroid containing varying amounts of thyroid hormones were used, but these have now been replaced with the use of levothyroxine monotherapy.[4]
- 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.[4]
- 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.[4]
- 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.[4]
- There is currently insufficient evidence of clinical and cost effectiveness to support the use of liothyronine (either alone or in combination) for the treatment of hypothyroidism.[5,6]
- Overwhelming evidence supports the use of thyroxine alone in the treatment of hypothyroidism, with this usually being prescribed as levothyroxine.[2]
- Liothyronine (available as licensed 20 microgram tablets and unlicensed 5 microgram tablets) is considerably more expensive than levothyroxine.[6] Many other liothyronine-containing preparations (such as Armour Thyroid) are also unlicensed, therefore the safety and quality of these products cannot be assured.
- Liothyronine is subject to supply issues and the amount of active ingredient may not be standardised so can vary from batch-to-batch, providing variable control.
- UK and international guidelines[5,8,9] found no consistently strong evidence for the superiority of alternative preparations (L-T4 + L-T3 combination therapy or thyroid extract therapy – preparations containing dried animal thyroid extracts, such as Armour Thyroid) over monotherapy with levothyroxine in improving health outcomes. It is recognised that some patients on levothyroxine remain symptomatic despite treatment leading to TSH levels in the therapeutic range. The reasons for this are not fully understood and such patients should be under the care of an endocrinologist.[2]
- The BTA does not recommend the routine prescribing of additional liothyronine in any presently available formulation, including Armour Thyroid, as it is inconsistent with normal physiology, has insufficient evidence to show that combination therapy is superior to L-T4 monotherapy, and may be harmful.[2] There is no evidence to support the use of L-T3 monotherapy.[2]
- However, the BTA statement advises that some patients, who have unambiguously not benefited from L-T4, may benefit from a trial of L-T4/L-T3 combination therapy.They should be supervised by accredited endocrinologists with documentation of agreement after fully informed and understood discussion of the uncertain benefits, likely risks of over-replacements and potential adverse consequences and lack of safety data.[2] The statement goes on to say that many clinicians may not agree that atrial of L-T4/L-T3 combination may be warranted in these circumstances and their clinical judgement must be recognised as being valid given the current understanding of the science and evidence of treatments.[2] A set of questions and answers relating to the statement that may help support discussion with patients is available here: http://www.btf-thyroid.org/images/documents/FAQ_for_BTA_Hypothyroidism_Statement.pdf
- 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

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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.

- Desiccated thyroid products (such as Armour Thyroid, ERFA) are unlicensed products in the UK, derived from pig thyroid, and contain an excessive amount of L-T3 in relation to L-T4
- Over-treatment with L-T4, when given alone, has similar risks to over-treatment with L-T3, e.g. palpitations and tremor, atrial fibrillation, strokes, osteoporosis and fracture. It is difficult to get dosing of L-T3 right and therefore the risk of over-treatment is high.[2]

Costs

There is a significant difference in cost between thyroid hormone replacement products. Table 1 on the following page illustrates the cost differences.

Table 1: Price comparison – Drug Tariff October 2015

Product	Cost per 28 tablets
Levothyroxine 25 microgram tablets	£3.11
Levothyroxine 50 microgram tablets	£2.12
Levothyroxine 100 microgram tablets	£2.11
Liothyronine 20 microgram tablets	£198.32
Other brands without a UK license ('specials')	£41 to £337 based on average cost per item (ePACT)

Switching options

Switch from liothyronine (including liothyronine-containing products) to the equivalent dose of levothyroxine, taking into account any other levothyroxine the patient is also co-prescribed and the patient's most recent thyroid function tests (TFT). The BNF states that 20–25 micrograms of liothyronine is equivalent to 100 micrograms of levothyroxine.[7] Patients should have repeat TFTs one to two months after switching to determine the appropriateness of their new dose.[7]

Patients under the care of a specialist endocrinologist should be referred back to consider suitability of switching in partnership.

Switch savings

There is a significant difference in cost between liothyronine-containing products and levothyroxine. Nationally, over £20.8 million is spent on liothyronine per year (ePACT May to July 2015).

Reducing liothyronine prescribing by 80% (including combination products with levothyroxine) could release savings of over £16.6 million nationally. This equates to savings of £ 29,123 per 100,000 patients.

Please note that the savings may be offset by levothyroxine costs for patients not already taking levothyroxine.

References

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Additional PrescQIPP resources



Audit and patient letter

Available at: http://www.prescqipp.info/resources/viewcategory/404-liothyronine

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