Liothyronine December 2018

Prescribing...

- Liothyronine is one of the products identified in the UK as being of low value and very high cost.
- The annual cost of prescribing liothyronine or L-T3 for about 16 patients was £57,000 in 2017.
- Prescribers are advised that all new patients requiring thyroid replacement should be, without exception, be started on levothyroxine or L-T4.
- Patients already on L-T3 should be switched to L-T4.
- Liothyronine will be removed from the White List on May 1st 2019.
- A small quantity of liothyronine will be kept for emergency use in the hospital.

Background

Liothyronine is a further example of an older product which has been subject to excessive price inflation. The cost has increased from £15.92 for 100 Tertroxin^{R} 20mg tablets in 2007 to £853 for 100 generic tablets in November 2018. In the UK the cost is in excess of £20 million per year and in the Bailiwick it is approximately £57,000 per year. This increase appears to have occurred only in the UK and not in other European countries. The Competition and Markets Authority is working to better understand why this has happened and to take action against companies where appropriate, but progress has been slow.

L-T3 vs L-T4

Levothyroxine (L-T4) is a prodrug and is converted to liothyronine (L-T3) in the body. 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. L-T4 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. Historically it was used in surgical patients who have had radioiodine. Radioiodine treatment required the patient's TSH to be high which meant bringing them off their replacement and Liothyronine was used because of its shorter half-life meaning that the myxoedematous period was much shorter. However, Thyrogen (recombinant TSH) is now used in preference. Bailiwick residents going to Southampton get two i.m. doses of Thyrogen on Saturday and Sunday prior to going over on Monday and this completely obviates the need to come off their L-T4 weeks in advance and the need to prescribe L-T3. So there should be no need to use the Liothyronine in the period between surgery and radioiodine therapy.

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. 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. Overwhelming evidence supports the use of thyroxine alone in the treatment of hypothyroidism, with this usually being prescribed as levothyroxine.

Safety and efficacy

Liothyronine (available as licensed 20 microgram tablets and unlicensed 5 microgram tablets) is considerably more expensive than levothyroxine. 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 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. 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.

The BTA does not recommend the routine prescribing of additional liothyronine in any presently available formulation, or 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. There is no evidence to support the use of L-T3 monotherapy.

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.

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.

Costs

There is a significant difference in cost between thyroid hormone replacement products. The average cost of a prescription for liothyronine 5 microgram tablets was **£504** per month or **£6,048** per patient per year. For Levothyroxine it was between **£1.88** and **£2.18.**

Switching options

The Prescribing and Formulary Panel has reviewed the evidence and is recommending that all patients on liothyronine are switched to levothyroxine. The BNF states that 20 to 25 micrograms of liothyronine is equivalent to approximately 100 micrograms of levothyroxine sodium. As always Consultant advice may be sought for individual patients or appointments arranged. Liothyronine will be removed from the Prscribing List on May 1st 2019.

Written by : Geraldine O'Riordan , Prescribing Advisor, Edward T Wheadon House, Le Truchot, St Peter Port GY13WH

References

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