British Thyroid Association
Encouraging the Highest Standards of Research and Patient Care

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BRITISH THYROID ASSOCIATION EXECUTIVE COMMITTEE
INFORMATION FOR MEMBERS ON PRESCRIBING LIOTHYRONINE (L-T3)

The BTA Executive Committee have been made aware of recent difficulties encountered by patients in obtaining Liothyronine (L-T3). In some instances, patients who have long been established on L-T3 have had their treatment abruptly withdrawn and some clinicians have received requests from local health authorities to switch patients from L-T3 to levothyroxine (L-T4). We are concerned that these actions are driven by cost considerations rather than clinical need and that the BTA position statement on the management of hypothyroidism is being inappropriately cited to support this requests. The BTA does not support the sudden withdrawal of L-T3 therapy and this practice does not in any way reflect our position statement. In this document we highlight current problems with L-T3 availability and offer advice to endocrinologists who may be asked to review patients with a view to stopping L-T3. Additional documents addressing frequently asked questions on this issue by General Practitioners [1] and patients [2] are available on the BTA website.

BTA position on the use of L-T3 in primary hypothyroidism

In 2015 the BTA executive committee published an evidence based position statement on the management of primary hypothyroidism [3]. L-T4 therapy remains the standard of care for hypothyroidism and offers a well-tolerated and effective treatment for the vast majority of patients. However, we recognise that a proportion of patients on L-T4 continue to suffer with symptoms despite adequate biochemical correction and that a carefully audited trial of L-T3 under the supervision of an accredited endocrinologist might be warranted in exceptional cases [3]. Thus, a small proportion of hypothyroid patients will be treated with L-T3 most of whom will be known to local endocrinology services. However, a fraction of patients, especially those who have been on L-T3 treatment for many years, may not attend secondary care clinics and endocrinologists may receive requests to review such patients with a view to discontinuing treatment. We wish to emphasise that the decision to continue or stop L-T3 should be based on

clinical need above other considerations and that the BTA position statement should in no way be used as an endorsement for discontinuing L-T3.

Price increases in L-T3

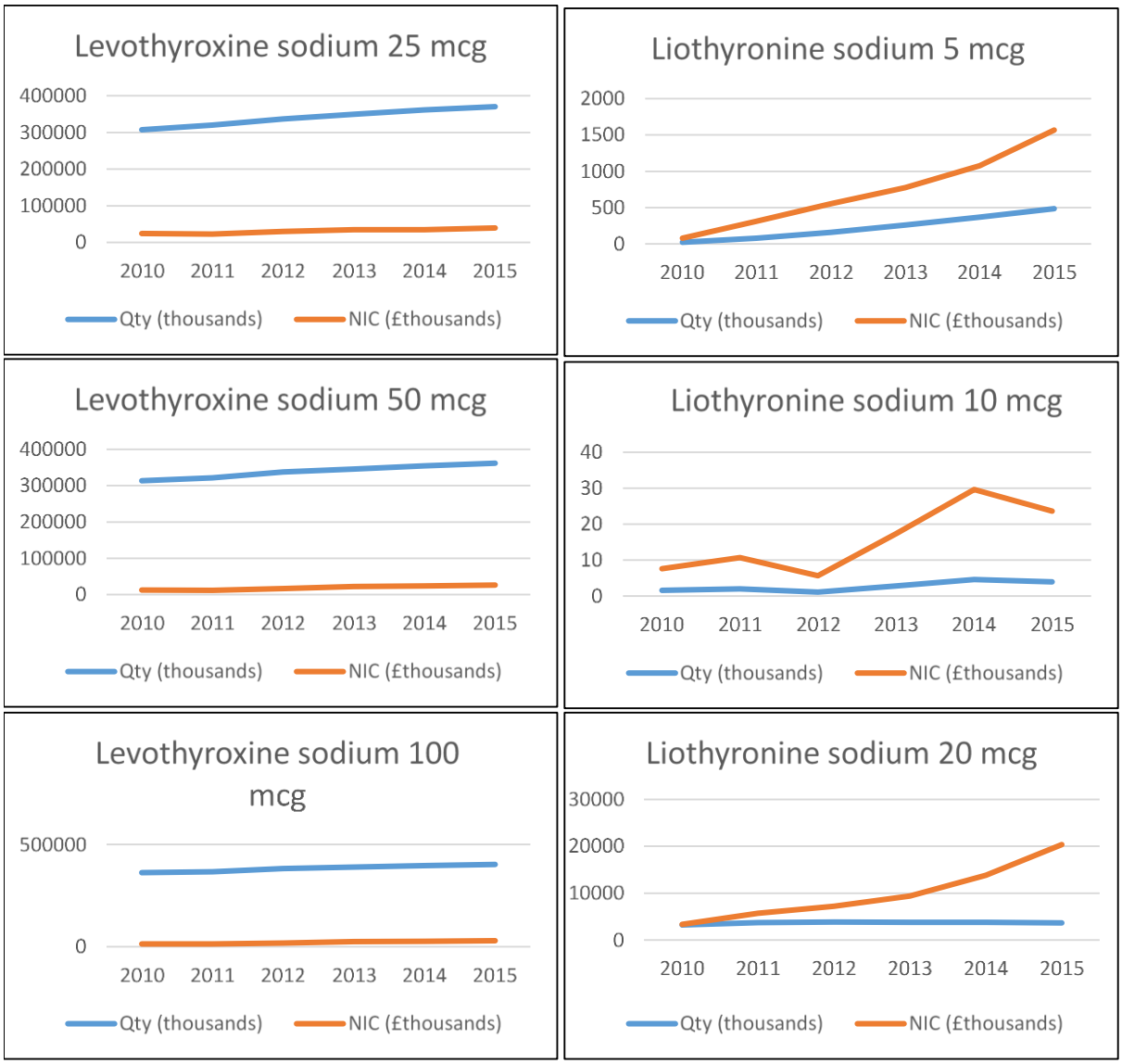
Recent years has seen a surge in L-T3 price to a magnitude in excess of 1000% (table 1-2). These increases appear to have arisen from exploitation of a loophole in the NHS pricing system. Generic NHS products are not price controlled, a measure that was designed to encourage competitive pricing but which can have the opposite effect. For example, where there is a limited number of suppliers for a product, such suppliers can unilaterally inflate prices. Several years ago, L-T3 was registered as a generic product with a sole NHS supplier and since then there has been a gradual increase in price, particularly in the last three years. This price rise is out of proportion to increases in the price of levothyroxine (L-T4) and involves the 28 day prescription cost to the patient (what it costs the pharmacy for individual prescriptions) as well as the net ingredient cost to the NHS overall. (Figures 1-3, tables 1-2). Furthermore, L-T3 price increases appears to have occurred in the UK relative to other European countries (Table 3). A Times newspaper investigation published in June 2016 highlighted this problem and subsequently, the health minister has ordered a review of the NHS pricing system by the competition watchdog, Competition and Markets Authority (CMA). The report of this review, due early next year, is likely to involve a change in current legislation to prevent unwarranted price increases.

Clinical approach to patients on L-T3

- For patients who are established on L-T3 and are considered to be stable, a change to L-T4 monotherapy should not be implemented without discussion with the patient. In such cases change of treatment may result in significant instability of thyroid status and potentially undesirable clinical outcomes, which may prove more costly than continuation with L-T3 therapy.
- For patients with hypothyroidism who are not on L-T3 but wish to be treated with L-T3, the principles in decision-making should follow those outlined in the BTA statement and in line with the best principles of good medical practice [3]. Combination treatments of L-T3 and L-T4 should only be initiated and supervised by accredited endocrinologists [3].

- In patients where it is agreed to switch from combined L-T3 and L-T4 treatment or from L-T3 monotherapy to L-T4 monotherapy, the transition should be made cautiously and gradually aiming to avoid under or over-replacement with thyroid hormones. The final L-T4 requirement is likely to be around 1.6µg/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.
- Because of the long half-life of L-T4, and the short half-life of L-T3, a “one-step, straight switch” from L-T3 to L-T4 may result in a phase of under-replacement, especially in patients who were previously treated with L-T3 monotherapy. Gradual reduction of L-T3 starting at the same time as introducing levothyroxine may be a preferable alternative. Frequent assessment of clinical and biochemical thyroid status is recommended until stability is reached. Awareness of the pharmacokinetics of L-T3 and L-T4 is important in interpreting thyroid function tests during the transitional period.
- In patients with a diagnosis of thyroid cancer where L-T3 is being recommended by clinical teams in preparation for radioiodine ablation, radioiodine therapy, diagnostic iodine scanning or stimulated thyroglobulin test, access to L-T3 is imperative and substitution with L-T4 is inappropriate (See BTA guidelines for the management of thyroid cancer [4]).
- L-T4/L-T3 combination therapy is not recommended in pregnancy.
- In patients over the age of 60, or of any age with known heart disease additional care is required to avoid over-replacement.

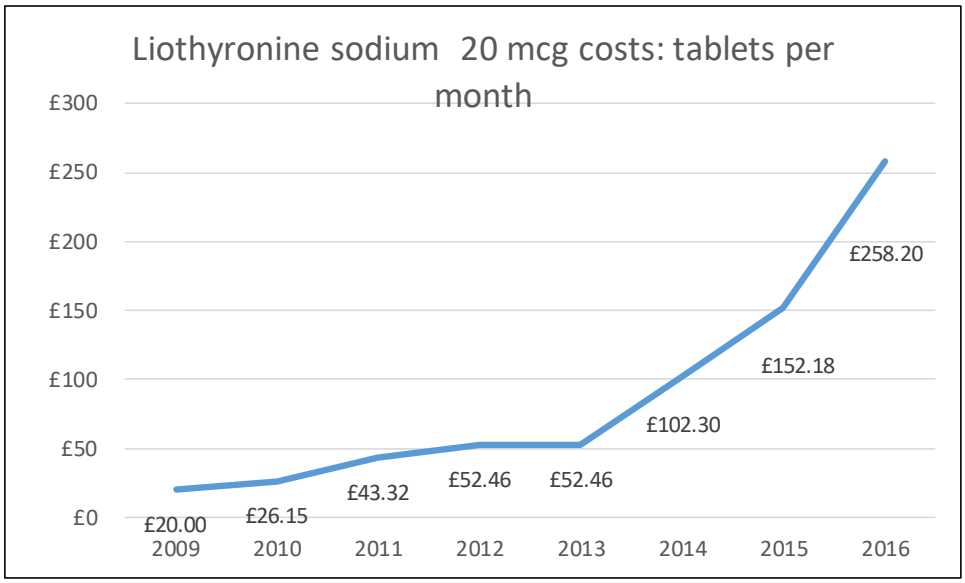
Figure 1: Quantity (in thousands) and net ingredient costs (NIC) (in thousands) of L-T4 and L-T3 2010-2015



Data from Prescription Cost Analysis England

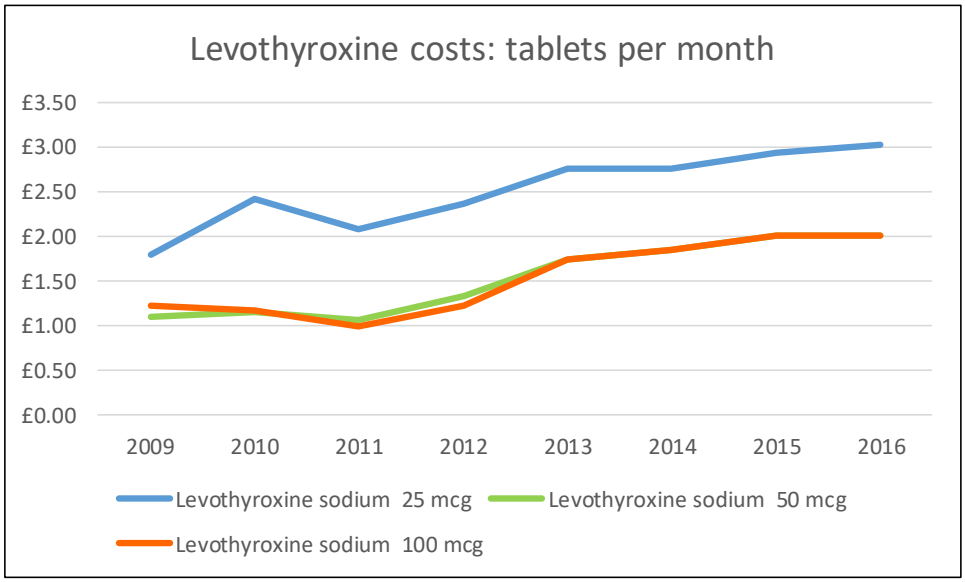
http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx

Figure 2: Costs of L-T3 from 2009-2016



Data from BNF and drug tariff

Figure 3: Costs of L-T4 from 2009-2016



Data from BNF and drug tariff

Table 1: Relative change in quantity prescribed and net ingredient costs (NIC) to NHS England, 2010–2015

	% change in Quantity	% change in NIC
Levothyroxine sodium 25µg	20	60
Levothyroxine sodium 50µg	15	115
Levothyroxine sodium 100µg	11	107
Liothyronine sodium 5µg	2045	1908
Liothyronine sodium 10µg	156	226
Liothyronine sodium 20µg	13	502

Data from Prescription Cost Analysis England http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx. L-T3 5µg and 10µg tablets are not available on the NHS but individual patients can obtain these strengths through special prescriptions in which case local pharmacies can source the required products from suppliers

Table 2: Relative change in costs of L-T3 and L-T4 from 2009–2016

Product	% change in costs
Levothyroxine sodium 25µg	68
Levothyroxine sodium 50µg	84
Levothyroxine sodium 100µg	66
Liothyronine sodium 20µg	1191

Data from BNF, drug tariff

Table 3: Costs of L-T3 in UK compared with France and Germany

Preparation	Country	Quantity	Cost	Source
Liothyronine sodium Concordia	UK	28 tablets	£258	Drug tariff
L-T3	France	30 tablets	€2,75	Personal communication; L-T3 user
L-T3, Thybon, Henning	Germany	100 tablets	€25.53	Personal communication; L-T3 user

References

1. BTA/BTF Frequently asked questions for patients
2. BTA/BTF Frequently asked questions for General practitioners
3. Okosieme, Gilbert J, Abraham P, et al. Management of primary hypothyroidism: statement by the British Thyroid Association Executive Committee. Clin Endocrinol (Oxf). 2016;84):799-808.
4. Perros P, Boelaert K, Colley S, et al. British Thyroid Association. Guidelines for the management of thyroid cancer. Clin Endocrinol (Oxf). 2014 Jul;81 Suppl 1:1-122.