NHS
Wakefield
Clinical Commissioning Group

Commissioning Statement

Treatment	**Liothyronine**
For the treatment of	Hypothyroidism
Commissioning position	**Wakefield CCG does not routinely commission the use of liothyronine monotherapy or combination therapy (including Armour thyroid®) in the long term treatment of hypothyroidism.** Liothyronine is only approved in the following circumstances: • Patients who are allergic to levothyroxine and thus liothyronine is the only treatment option to manage their condition. • Post thyroidectomy thyroid cancer and non-cancer patients. Patients that need to receive radioactive iodine treatment after their surgery will initially be started on liothyronine due to its shorter half-life and therefore faster onset of action. These patients will be switched to levothyroxine when the course of radioactive iodine treatment is completed. • In patient treatment of profound hypothyroidism under the care of and/or direction of an endocrinology expert. Patients commenced on liothyronine therapy before the publication of this commissioning statement may continue their treatment until they and their clinician consider it appropriate to stop.
Date effective from	13th July 2017
Policy to be reviewed by	28th February 2020
Background information	Hypothyroidism, underactivity of the thyroid gland, is common. It can make people unwell and should be treated with levothyroxine tablets, a synthetic form of the thyroid hormone thyroxine (T4). This is the treatment 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 (T3) is the active thyroid hormone and the majority is produced by peripheral conversion of levothyroxine (T4) but it is a much shorter half-life and steady state cannot be maintained with once daily dosing. The Royal College of Physicians does not recommend the prescribing of liothyronine for the management of primary hypothyroidism, as it is inconsistent with normal physiology, has not been

	unequivocally proven to be of any benefit to patients, and may be harmful. Data suggest that 5–10% of levothyroxine treated hypothyroid patients with normal serum TSH have persistent symptoms. There are several suggested explanations for this, but an inadequacy of levothyroxine to restore physiological T4 and T3 concentrations in serum and tissues and the existence of levothyroxine conversion disorders have been used as explanations in support of liothyronine treatment.
Summary of evidence/ rationale	The combination of levothyroxine and liothyronine, in both non-psychological and physiological proportions, has not consistently been shown to be more beneficial than levothyroxine alone with respect to cognitive function, social functioning and wellbeing. UK and international guidelines found no consistently strong evidence for the superiority of alternative preparations (T4 + T3 combination therapy or thyroid extract therapy – preparations containing dried animal thyroid extract therapy, such as Armour Thyroid) over monotherapy with levothyroxine in improving health outcomes. A study that investigated the effect of liothyronine treatment in patients with different genotypes for liothyronine conversion (deiodinase) enzymes has been quoted in support of the existence of a conversion disorder. A small number of patients with a certain genotype of the deiodinase 2 gene had worse psychological well-being at baseline and had greater improvements from liothyronine compared to placebo. No differences between genotypes in effects on thyroid function tests were seen. It is postulated that as deiodinase 2 is the only version of the enzyme able to convert T4 in the brain, certain genotypes may result in a poorer psychological response to T4 despite normalisation of thyroid function tests. **Genotype testing is not currently available in clinical practice and this study concludes that replication of the result is required before changes in treatment approach can be recommend in routine practice.** The British Thyroid Association statement makes the following comment about genetic testing : it is not recommended as a guide to selecting therapy for the following reasons: • Although there are data suggesting that specific polymorphisms of the type 2 deiodinase gene might be associated with therapeutic response to combination synthetic T3 and T4 therapy, controlled confirmatory studies are needed. • The small effect of the type 2 deiodinase gene variants identified so far that do affect thyroid hormone concentrations suggests that other factors may play a far greater role in determining an individual patient's thyroid hormone concentrations.

	Cost effectiveness: The cost of liothyronine is significantly greater than levothyroxine.
References	Summary of product characteristics liothyronine 20microgram tablets (Concordia International) available from http://www.medicines.org.uk/emc/medicine/25628 Drug Tariff. August 2016 Available from http://www.drugtariff.nhsbsa.nhs.uk/#/00336026-DD_1/DD00336022/Home The diagnosis and management of primary hypothyroidism © Royal College of Physicians 2011 http://www.rcplondon.ac.uk/sites/default/files/the-diagnosis-and-management-of-primary-hypothyroidism-revised-statement-14-june-2011_2.pdf British Thyroid Association Executive Committee: Management of primary hypothyroidism 2015 http://www.british-thyroid-association.org/news/BTA_Hypothyroidism_Statement.pdf American Thyroid Association: Guidelines for the Treatment of Hypothyroidism: 2014 http://online.liebertpub.com/doi/pdf/10.1089/thy.2014.0028 PrescQIPP DROP-List Bulletin February 2016. https://www.prescqipp.info/news/newsfeed/bulletin-121-updated-liothyronine-drop-list UKMI Q&A 56.7: What clinical evidence is there to support the use of "Armour thyroid" or other desiccated thyroid extract products? February 2016 https://www.sps.nhs.uk/articles/what-clinical-evidence-is-there-to-support-the-use-of-oarmour-thyroido-or-desiccated-thyroid-extract/ Panicker V et al. Common variation in the DI02 gene predicts baseline psychological well-being and response to combination thyroxine plus triiodothyronine therapy in hypothyroid patients. J Clin Endocrinol Metab, 2009; 94(5): 1623-1629. http://press.endocrine.org/doi/abs/10.1210/jc.2008-1301
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Cost

Liothyronine currently costs approximately £3,000 per patient per year based on a 10microgram twice daily dosing. A 100microgram dose of levothyroxine costs approximately £23 per patient per year.

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