VERDICT
The Area Prescribing Committee recommends that liothyronine is prescribed only by the specialist. The committee recognises that some patients have been established on the product for a considerable time and this may be difficult to change. Hence there will be some legacy prescribing in primary care. However all those newly started on liothyronine should be under specialist supervision and should be changed to levothyroxine for routine therapy when primary care prescription is requested.

Specialist Drugs List Status: Specialist Only (SO)

SUMMARY NOTES

Indication\(^1\): Used for the treatment of coma of myxoedema, the management of severe chronic thyroid deficiency and hypothyroid states occurring in the treatment of thyrotoxicosis. Liothyronine sodium can be used also in the treatment of thyrotoxicosis as an adjunct to carbimazole to prevent sub-clinical hypothyroidism developing during treatment. Liothyronine sodium may be preferred for treating severe and acute hypothyroid states because of its rapid and more potent effect, but levothyroxine sodium is normally the drug of choice for routine replacement therapy.

Pharmacological action\(^1\): Liothyronine sodium is a naturally occurring thyroid hormone. The biological action of Liothyronine sodium is quantitatively similar to that of Levothyroxine sodium, but the effects develop in a few hours and disappear within 24 to 48 hours of stopping treatment. 20 – 25 micrograms is equivalent to 100 micrograms of levothyroxine\(^2\)

Presentation: Each tablet contains 20 micrograms liothyronine sodium BP\(^1\)

Dose: Baseline ECG is valuable with initial dosage because changes induced by hypothyroidism can be confused with ischaemia.\(^1\)

Adults: Starting dose of 10 or 20 micrograms every 8 hours, increasing after one week, if necessary, to the usual recommended daily dose of 60 micrograms in two or three divided doses.

Myxoedema Coma: 60 micrograms given by stomach tube, then 20 micrograms every 8 hours. It is more usual to start treatment with intravenous liothyronine.

Adjunct to carbimazole treatment of thyrotoxicosis: 20 micrograms every 8 hours.

Elderly and Children Patients: 5 micrograms daily (Liothyronine sodium tablets can be crushed and triturated with lactose for administration as a powder).

Cost comparison: (these doses are for general comparison and do not imply therapeutic equivalence):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose Regimen</th>
<th>Cost per 28 days(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liothyronine</td>
<td>20 microgram</td>
<td>£206.71</td>
</tr>
<tr>
<td>Levothyroxine</td>
<td>50/100 microgram</td>
<td>£1.03</td>
</tr>
<tr>
<td>Levothyroxine</td>
<td>50 microgram</td>
<td>£1.63</td>
</tr>
</tbody>
</table>

DRUG PROFILE

Clinical Effectiveness: There appears to be no robust evidence on the use of liothyronine either alone or in combination with levothyroxine. A review of fourteen hypothyroid patients\(^4\) evaluated the efficacy of thyroid hormone replacement with L-T4 or L-T3 at doses producing equivalent normalization of TSH. L-T3 or L-T4 were administered thrice daily to achieve a target TSH from 0.5 to 1.5 mU/litre. Volunteers were studied as inpatients after 6 weeks on a stable dose and at the target TSH.

The main outcome measures were Serum thyroid hormones, lipid parameters, and indices of glucose metabolism. Results showed no difference observed in TSH between L-T3 and L-T4 treatments. L-T3 resulted in significant weight loss [L-T4, 70.6 ± 12.5, vs. L-T3, 68.5 ± 11.9 kg (P = 0.009)] and in a 10.9 ± 10.0% decrease in total cholesterol (P = 0.002), 13.3 ± 12.1% decrease in low-density lipoprotein-cholesterol (P = 0.002), and an 18.3 ± 28.6% decrease in apolipoprotein B (P = 0.018). No significant differences were observed in high-density lipoprotein-cholesterol, heart rate, blood pressure, exercise tolerance, or insulin sensitivity.
A large, double-blind, randomized controlled trial\(^5\) (n=697 hypothyroid patients) examined partial substitution of 50 mcg T4 by 10 mcg T3 vs. the original dose of T4. The results showed transient improvement after partial substitution with T3 but did not provide conclusive evidence of specific benefit from partial substitution of T4 by T3 in patients on T4 replacement. The authors also concluded that the study emphasised the large size and sustained nature of the placebo effect that may be obtained in studies of this nature.

CKS\(^6\) does not recommend the use of liothyronine in patients with overt hypothyroidism. A UKMi\(^7\) review summarised that there is a lack of good quality evidence to support the use of desiccated thyroid. Studies vary in design, size, duration and outcomes. There is only one small randomised, controlled, crossover trial which has compared the efficacy of desiccated thyroid with levothyroxine. Seventy patients were treated with one treatment for a period of 16 weeks, then crossed over to the other treatment for another 16 weeks. There was no difference in general health and all patients had TSH levels within range. Patients who preferred desiccated thyroid (49%) tended to have greater weight loss and improvement in subjective symptoms such as concentration, memory and energy. The review added that whilst some patients do request treatment with desiccated thyroid, such as AT because they do not feel as well when treated with levothyroxine, but there is a lack of robust evidence supporting the clinical effectiveness of desiccated thyroid. The NHS England document *Items which should not be routinely prescribed in primary care* advise against the use of liothyronine (including Armour\(^8\) Thyroid) except under exceptional circumstances when levothyroxine has failed and use is supported by a consultant NHS endocrinologist. The Regional Medicines Optimisation Committee (RMOC) gives further guidance to prescribers around exceptional circumstances, criteria and responsibilities for liothyronine prescribing.\(^9\)

**Safety**

Adverse effects: The following effects\(^1\) are indicative of excessive dosage and usually disappear on reduction of dosage or withdrawal of treatment for a day or two. Anginal pain, cardiac arrhythmias, palpitations, muscle cramps, tachycardia, diarrhoea, restlessness, excitability, headache, flushing, sweating, excessive loss of weight and muscular weakness, vomiting, tremor, insomnia, fever, heat intolerance, transient hair loss in children, hypersensitivity reactions including rash, pruritus and oedema also reported.

Elderly: In myxoedema, care must be taken to avoid imposing excessive burden on cardiac muscle affected by prolonged severe thyroid depletion. Care is needed in the elderly.

**Cautions/Contra-indications:** Patients with angina of effort or cardiovascular diseases and thyrotoxicosis. Hypersensitivity to any components of Liothyronine sodium tablets.

**CURRENT PLACE IN THERAPY**

National institute for Health and Care Excellence (NICE) - no guidance

Scottish Medicines Consortium (SMC) - no guidance

Midlands Therapeutics Review and Advisory Committee (MTRAC) - no guidance

The British Thyroid Association (BTA) position statement\(^6\) on the management of primary hypothyroidism states that the routine use of thyroid extracts, L-T3 monotherapy, compounded thyroid hormones, iodine containing preparations, dietary supplementation, nutraceuticals and over the counter preparations are not recommended in the management of hypothyroidism. This guideline is endorsed by the Royal College of Physicians (RCP). L-T4 is the treatment of choice in hypothyroidism. The goal of therapy is to restore physical and psychological well-being and normalise serum TSH.

Regional Medicines Optimisation Committee (RMOC) – In most cases, the primary care prescribing of liothyronine (T3) is not supported for any patient and recommends that strict criteria are applied to ensure that liothyronine is only prescribed in the very rare situations where alternative treatments have been found to be inadequate.\(^9\)

**Summary**

- The RCP\(^5\) and RMOC do not support the use of thyroid extracts or levothyroxine and T3 combinations without further validated research published in peer-reviewed journals.

- RMOC states that in most cases, primary care prescribing of liothyronine is not supported and strict criteria should be applied to ensure only prescribing in those rare situations where alternative treatments have been found to be inadequate.\(^9\)

References