

Liothyronine (T3) for the combination treatment (T3 + Levothyroxine (T4)) of Hypothyroidism in a selected cohort of adults **Amber with shared care**

Shared Care Guidelines: Liothyronine (T3) for the combination treatment (T3 plus T4) of hypothyroidism

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of medicine name and indication shared between the specialist and general practitioner (GP). GPs are **invited** to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with the condition are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

Specialist responsibilities	
1	Ensure the patient fulfils the criteria for treatment.
2	Ensure that all alternative causes of symptoms have been excluded.
3	Prescribe, monitor and assess response biochemically and assess physical and psychological wellbeing after at least 3 months of treatment and until treatment dose is stabilised.
4	Discuss the benefits and side effects of treatment with the patient.
5	Ask the GP whether he or she is willing to participate in shared care and agree with the GP as to who will discuss the shared care arrangement with the patient.
6	Supply GP with summary within 14 days of a hospital out-patient review or in-patient stay.
7	Give advice to the GP on monitoring and when to stop treatment.
8	Review the patient's condition and monitor response to treatment regularly where indicated.
9	Report adverse events to the MHRA.
10	Ensure that clear backup arrangements exist for GPs to obtain advice and support.

General Practitioner responsibilities	
1	Reply to the request for shared care as soon as practicable if they are unable to support shared care (in writing or via secure email).
2	Prescribe liothyronine (T3) in line with shared care guidance once a stable dosing regimen has been determined by specialist care and monitor as recommended.
3	Monitor biochemistry periodically as recommended by the specialist. Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
4	Liaise with specialist regarding any complications of treatment and stop treatment on the advice of the specialist.
5	Report to and seek advice from specialist on any aspect of patient care of concern to the GP that may affect treatment.
6	Ensure no drug interactions with concomitant medicines that are added later.
7	Report adverse events to the specialist and MHRA.

Patient's role	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine.
4	Attend GP/specialist appointments for regular monitoring.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Fax:	Email address:
RUH via Cinapsis	-	-	Use Cinapsis app
GWH endocrinology secretaries	01793 604313	0179360450	gwh.diabetessecretaries@nhs.net
SFT via Cinapsis	-	-	Use Cinapsis app

Monitoring

- Monitoring is by TSH levels measured from blood tests taken prior to the morning medication.
- Initial biochemical monitoring will be undertaken by the specialist until the dose is stable.
- Initially and following a dose change a repeat test will be required at 6-8 weeks. After dose stabilisation, monitoring should only be required annually unless there is a change in symptoms that may warrant the checking of TSH levels.
- The aim of the treatment is to maintain TSH of 0.4-2.5mU/L with the T3 and T4 in the normal range.

Parameter	Action (adjustment and referral back to hospital)
More than 5 mU/L	Increase levothyroxine dose by 25 micrograms.
0.4-5.0 mU/L	No change required.
Less than 0.4 mU/L	Seek specialist advice, likely resume at lower dose.

SUPPORTING INFORMATION

The medicine is indicated for:

Liothyronine/Levothyroxine (T3/T4) combination therapy

Combination liothyronine/levothyroxine (T3/T4) should not be used routinely in the management of hypothyroidism as there is insufficient population based clinical evidence to show that combination therapy is superior to levothyroxine (T4) monotherapy. As part of the overall holistic management of patients with hypothyroidism, NHS consultant endocrinologists may start a trial of combination liothyronine/levothyroxine (T3/T4) in circumstances where all other treatment options have been exhausted.

1. Where symptoms of hypothyroidism persist despite optimal dosage with levothyroxine. (TSH 0.4-1.5mU/L)
2. Where alternative causes of symptoms have been excluded.

Exclusions.

1. Patients with thyroid cancer who need liothyronine (T3) as part of their investigation and treatment will remain under the specialist care.
2. Women who are planning pregnancy who are taking liothyronine (T3) should remain under specialist care as it is not recommended in pregnancy.
3. In rare cases where liothyronine (T3) is used for resistant depression, therapy should be supervised by a consultant psychiatrist. This is off licence and not approved locally.

Treatment Aims (Therapeutic plan)

In most circumstances, the primary care prescribing of liothyronine (T3) is not supported for any patient. Initiation for patients with hypothyroidism should only be undertaken by consultant NHS endocrinologists. This advice applies to both liothyronine (T3) monotherapy and combination therapy with levothyroxine (T3/T4). As specified by the British Thyroid Association Executive Committee, 'clinicians have an ethical responsibility to adhere to the highest professional standards of good medical practice rooted in sound evidence. This includes not prescribing potentially harmful therapies without proven advantages over existing treatments.' Therefore, strict criteria should be applied to ensure that liothyronine (T3) is only prescribed in the very rare situations where alternative treatments have been found to be inadequate.

Treatment Schedule (including dosage and administration)

Liothyronine (T3) should only be prescribed as part of a combination treatment with levothyroxine (T4).

When liothyronine (T3) is commenced, a reduction in levothyroxine (T4) dose will be required. Specialists should individualise approach to dose changes. Typically, for every 10micrograms of liothyronine (T3) the levothyroxine (T4) dose should be reduced by 50micrograms. (e.g., levothyroxine 125micrograms each morning would become 75micrograms levothyroxine (T4) each morning and 10micrograms liothyronine (T3) each morning).

Response may be assessed via pre and post symptom scoring or quality of life (QoL) questionnaire. A thyroid specific QoL tool will not be available for some time. Some of the original research papers for T3 used the [SF36 tool](#) as a measure of improvement in well-being however some endocrinology consultants do not consider SF36 suitable for hypothyroid patients and may not wish to use a QoL questionnaire at all.

For patients that do not benefit from liothyronine (T3) and require converting back to levothyroxine (T4), the specialist should advise on an individualised approach to switching. The BNF states that 20-25 micrograms of liothyronine (T3) is approximately equivalent to 100micrograms levothyroxine (T4).

Contra-indications and precautions for use

Liothyronine (T3) is **contraindicated** in: (Discuss with NHS Endocrinologist)

- Known hypersensitivity to the drug or any of its excipients
- Thyrotoxicosis
- Cardiac arrhythmias
- Angina
- Pregnancy

Liothyronine (T3) should be **used with caution** in patients with:

- Ischaemic heart disease: any new presentation or significant worsening of existing ischaemic heart disease should be discussed with the specialist endocrinology team.
- Breast feeding: an increase in monitoring of thyroid function tests may be required, discuss with specialist endocrinology team.

Side-effects

Most serious toxicity is seen with long-term use and may therefore present first to GPs. Adverse events are usually seen at excessive dosage.

- Angina, arrhythmia: GP to stop liothyronine (T3) and check TSH.
- Palpitations, restlessness, tremor, diarrhea, headache, muscle cramps: GP to continue liothyronine (T3) and check TSH.

The GP should advise the patient that taking too much liothyronine (T3) may cause agitation, confusion, headache, sweating and a rapid pulse. If you take too many tablets, contact your doctor or nearest hospital casualty department as soon as possible.

Refer to the SPC for a full list of adverse effects. Liothyronine (T3) does not have black triangle (▼) status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.

Drug Interactions

- Liothyronine may potentiate the action of **anticoagulants**.
- **Anticonvulsants**, such as carbamazepine and phenytoin enhance the metabolism of thyroid hormones and may displace thyroid hormones from plasma proteins. Initiation or discontinuation of anticonvulsant therapy may alter liothyronine dose requirements. Phenytoin levels may be increased by liothyronine. Metabolism of thyroid hormones is accelerated by barbiturates and primidone and may increase requirements for thyroid hormones in hypothyroidism.
- If co-administered with **cardiac glycosides**, adjustment of dosage of cardiac glycoside may be necessary.
- Gastrointestinal absorption of thyroid hormones may be reduced by concurrent use of **antacids, sucralfate, iron, colestyramine or colestipol**.
- Liothyronine raises blood sugar levels and this may upset the stability of patients receiving **antidiabetic agents**.
- Co-administration of **oral contraceptives** may result in an increased dosage requirement of liothyronine sodium.
- **Amiodarone** is predicted to increase the risk of thyroid dysfunction when given with thyroid hormones.
- Thyroid hormones may enhance the effects of tricyclic antidepressants, notably **amitriptyline** and **imipramine**.
- A number of drugs may affect thyroid function tests and this should be borne in mind when monitoring patients on liothyronine therapy.

This list is not exhaustive. The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

Information on Preferred Formulation and Cost

May 2022 update: Liothyronine 5, 10 and 20 microgram **capsule** formulations are [now available](#) and are significantly more cost-effective than tablets in primary care. Acute trusts may still be using tablets under existing procurement contracts. When GPs take on long-term prescribing in primary care, patients should be switched from tablet formulation if used in acute trusts and the prescription should specify capsules. The tablets and capsules are bioequivalent. Table below indicates potential cost implications if liothyronine tablets are continued in primary care:

Formulation	Liothyronine 5microgram Capsules	Liothyronine 10microgram Capsules	Liothyronine 20microgram Capsules	Liothyronine 5microgram Tablets	Liothyronine 10microgram Tablets	Liothyronine 20microgram Tablets
	SUITABLE FOR PRESCRIBING IN PRIMARY CARE			NOT FOR PRESCRIBING IN PRIMARY CARE		
NHS indicative Price per pack size 28 caps/tabs	£55.00	£65.00	£55.00	£98.00 - £100.94	£148.00 - £152.44	£71.90 - £245.29

References

Summary of Product Characteristics: Liothyronine sodium 5, 10 and 20 micrograms capsules
<https://www.medicines.org.uk/emc/search?q=liothyronine+capsules> accessed online on 06/05/2022

Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press.
<http://www.medicinescomplete.com> accessed online on 06/05/2022.

Document details

Prepared by: Rachel Hobson and Jill Forrest. Formulary pharmacists. Based on original work by Basingstoke, Southampton & Winchester DPC which is included in the RMOG Guidance – Prescribing of liothyronine.

<https://www.sps.nhs.uk/medicines/liothyronine/#:~:text=liothyronine> accessed online on 06/05/2022

Date written: January 2019. Contact details updated September 2019. Information on formulations added May 2022. Contact details updated Oct 22.

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