Shared Care Protocol

Use of Liothyronine (T3) for the treatment of hypothyroidism in selected cohort of adults despite optimal dosage with levothyroxine and where alternative cause of symptoms have been excluded.

Shared Care Protocol developed by:

Dr Amit Allahbadia, Consultant Endocrinologist, Sheffield Teaching Hospitals.

Dr Simon Berry, Honorary Specialist Registrar, Sheffield Teaching Hospitals.

Barbara Obasi, Clinical Effectiveness Lead Pharmacist, South Yorkshire ICB Medicines Optimisation Team.

Approved by: South Yorkshire Integrated Medicine Optimisation Committee (IMOC)

Approval Date: August 2024

Review Date: August 2029

For patients within adult services

Specialist responsibilities

- Establish the clinical need for the drug.
- Assess the patient and provide primary care clinicians with diagnosis, relevant clinical information, baseline results, treatment to date, treatment plan and duration of treatment before specialist review.
- Conduct required baseline investigations and initial monitoring (see section 8).
- Ensure that the diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision-making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 3 months and until optimised.
- Once treatment is optimised, complete the shared care documentation, and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the Primary Care Clinician.
- Patients will be reviewed in the endocrine clinic in accordance with the recommendations of Hospital Specialist with a minimum frequency of every six months.
- Conduct the required reviews and monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 8 remains appropriate.
- Provide advice to primary care on the management of adverse effects if required.
- Patient to remain under the care of the specialist for the duration of the treatment which in most cases would be lifelong.

Primary care responsibilities

Back to top

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of receipt of the request, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists' request and as per section 5, taking into any account potential drug interactions that are added at a later time to initiation in section 7.
- Conduct the required monitoring as outlined in section 8. Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Stop treatment as advised by the specialist.
- Ensure secondary care specialist is notified if unwilling to undertake prescribing and monitoring when requested.

Patient and/or carer responsibilities

- Take liothyronine as prescribed and avoid abrupt withdrawal unless advised by their primary care clinician or specialist.
- Attend routine monitoring and review appointments with primary care and specialist.
- Keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend review appointments.
- Patient of childbearing potential should take a pregnancy test if they think they could be pregnant. They must contact the specialist endocrinology team or their GP in the case of becoming pregnant or if thinking of becoming pregnant.
- Report adverse effects to their primary care prescriber or specialist. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of liothyronine with their pharmacist before purchasing any OTC medicines.

1. Background

Back to top

Liothyronine is used to treat hypothyroidism. It has a similar action to levothyroxine but is more rapidly metabolised and has a faster effect. It is sometimes used in combination with levothyroxine. However, there is limited evidence for its efficacy above levothyroxine. Due to the significant costs associated with liothyronine and the limited evidence to support its prescribing in preference to levothyroxine, it should not routinely be prescribed in primary care. In terms of safety, due to the limited data on liothyronine use, the long-term adverse effects are uncertain and warrant further study. Liothyronine is contraindicated in patients

with ischaemic heart diseases. TSH levels should be monitored during treatment, and FT3 and FT4 levels where clinically appropriate, in order to reduce the risk of over or under-treatment. The risks of over-treatment include atrial fibrillation, osteoporosis, and bone fractures. In 2019, NICE (NG145) recommended that liothyronine should not be routinely offered for primary hypothyroidism, either alone or in combination with levothyroxine, because there is not enough evidence that it offers benefits over levothyroxine monotherapy, and its long-term adverse effects are uncertain.

In August 2023, NHSE issued a document entitled "Liothyronine-advice for prescribers", which provides detailed advice in relation to where and when it may be appropriate to prescribe liothyronine on the NHS for current and new patients with hypothyroidism, depression, and thyroid cancer. This updates previous guidance produced by the Regional Medicines Optimisation Committee (RMOC) published in 2019, and is in line with the "Use of liothyronine (T3) in hypothyroidism: Joint British Thyroid Association/ Society for endocrinology consensus statement on the use of liothyronine (T3) in hypothyroidism", published in June 2023.

Other thyroid preparations

The prescribing of unlicensed liothyronine, thyroid extract products (e.g., Armour thyroid, ERFA Thyroid), compounded thyroid hormones, iodine-containing preparations and dietary supplementation for primary hypothyroidism are not recommended as the safety, quality and efficacy of these products cannot be assured.

2. Indications

Back to top

- **Hypothyroidism in adults receiving liothyronine co-prescribed with levothyroxine.**
    - Levothyroxine co-prescribed with liothyronine 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 monotherapy.

    - As part of the overall holistic management of patients with hypothyroidism, NHS Consultant Endocrinologists may initiate a trial of levothyroxine co-prescribed with liothyronine in circumstances where all other treatment options have been exhausted and other conditions have been excluded as a cause of a patient's symptoms (see section 3).

- **Hypothyroidism in adults receiving liothyronine monotherapy.**
  Liothyronine monotherapy is not recommended in hypothyroidism.
  Prescribing would be in exceptional circumstances only, such as clearly distinguishable specific levothyroxine medication intolerance including extremely rare cases of

levothyroxine induced liver injury or potentially for patients who do not effectively metabolise levothyroxine to liothyronine, if a specialist assessing the patient according to these guidelines deems this to be necessary.

- Where symptoms of hypothyroidism persist despite optimal dosage with levothyroxine, please ensure TSH remains above the lower limit of the reference range for each locality as this may differ. Please refer to appendix 1 for some possible causes of persistent symptoms in euthyroid patients.

3. Exclusions (criteria where patients should remain under specialist care)

Back to top

1. Patients with thyroid cancer who need liothyronine as part of their investigation and treatment will remain under the specialist care.
2. Liothyronine should not be used in patients planning pregnancy unless in exceptional circumstance where the patient may be intolerant of levothyroxine after a discussion with the endocrinologist/obstetrician.
3. In rare cases where liothyronine is used for resistant depression, therapy should be supervised by a consultant psychiatrist. This is off licence.

Therefore, the use of liothyronine for indications other than hypothyroidism is out-with the scope of this guidance.

4. Contraindications and cautions

Back to top

This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Known hypersensitivity to the drug or any of its excipients.
- Thyrotoxicosis
- Cardiac arrhythmias
- Ischaemic heart disease
- Pregnancy

Cautions:

- Adrenocortical insufficiency: in severe and prolonged hypothyroidism, adrenocortical activity may be decreased. When thyroid replacement is started, metabolism increases more than adrenocortical activity. This can lead to adrenocortical insufficiency requiring supplemental adrenocortical steroids.
- Ischaemic heart disease: any new presentation or significant worsening of existing ischaemic heart disease should be discussed with the specialist endocrinology team.

5. Initiation and ongoing dose regime

Back to top

- Transfer of prescribing to primary care is normally after the patient has been initiated on treatment and evidence of clinical benefit of treatment confirmed after a period of at least 3 months.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

6. Pharmaceutical aspects in adults Back to top

Route of administration:	Oral
Formulation:	Tablets: 5 microgram, 20 microgram Capsule: 5, 10 and 20 micrograms * Liothyronine is significantly more expensive than levothyroxine therapy. Hence, the product with the lowest acquisition cost should be prescribed unless specific patient factors require another formulation.
Administration details:	Liothyronine Sodium Capsules/ Tablets are taken by mouth. They should be swallowed with a glass of water and to leave a gap of at least 30 minutes before eating or drinking any caffeinated beverages. Avoid iron or calcium supplementation for at least 3 hours. If a patient has difficulty swallowing a whole tablet, the tablet may be crushed and allowed to dissolve/disperse in at least 20 mL of water. The entire volume of liquid should be consumed to ensure the full dosage is taken.
Other important information:	**When co-prescribed with levothyroxine:** When liothyronine is commenced a reduction in levothyroxine dose will be required. Specialists should individualise approach to dose changes, however typically, for every 10 micrograms of liothyronine, the levothyroxine dose should be reduced by 25micrograms.

7. Significant medicine interactions
Back to top

The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

- Anticonvulsants: Phenytoin levels may be increased by liothyronine. 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.
- Requirements for thyroid hormones in hypothyroidism may be increased by oestrogens.
- Digoxin: liothyronine is predicted to affect the concentration of digoxin. Manufacturer advises monitor and adjust dose.
- Liothyronine may result in an increase in insulin or anti-diabetic drug requirements.

8. Baseline investigations, initial monitoring, and ongoing monitoring to be undertaken by specialist Back to top

- Initial biochemical monitoring will be undertaken by the specialist until a stable regimen is established. Shared care will only be requested once stable regimen established.
- Please ensure that the patient is in sinus rhythm before initiating and during treatment with liothyronine.
- Monitoring is by serum TSH, FT4, FT3 levels measured from blood tests taken 2-4 hours after the morning dose of liothyronine/levothyroxine.
- Initially and following a dose change a repeat test will be required at 6-8 weeks following this change. After dose stabilisation, monitoring should only be required 6 monthly unless there is a change in symptoms, comorbidities or concurrent medication that may warrant the checking of TSH levels.
- The aim of the treatment is to maintain TSH (and where appropriate T3 and T4) within the normal range. Secondary care will undertake twice yearly reviews with the patient to ensure treatment is still indicated.

9. Ongoing monitoring requirements to be undertaken by primary care
Back to top

See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring	Frequency
No routine monitoring is required by primary care	

10. Adverse effects and other management
Back to top

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

The long-term use of thyroid hormone therapy can result in serious toxicity, which may therefore first present to GPs. Over-treatment with thyroid hormones may lead to atrial fibrillation, osteoporosis, and bone fractures, while the risk of under-treatment also poses significant risks. Therefore, if levels are outside of the normal laboratory reference range, it is recommended to seek advice from the specialist endocrinologist.

Result	Action for primary care
Angina, arrhythmia	Stop liothyronine, check TSH, FT4, FT3 (if available). Primary care clinician to contact managing endocrinologist.
Other symptoms of excessive dose: palpitations, restlessness, anxiety, tremor, diarrhoea, headache, muscle cramps	Continue liothyronine, check TSH, FT4, FT3 (if available). Primary care clinician to contact managing endocrinologist.

11. Advice to patients and carers

Back to top

The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

Chest pain, palpitations, restlessness, anxiety, tremor, diarrhoea, headache, muscle cramps**.**

12. Pregnancy, paternal exposure and breast feeding

Back to top

It is the responsibility of the specialist to provide advice on the need for contraception to female patients on initiation and at each review.

Pregnancy:

- Safety during pregnancy is not known. The risk of foetal congenital abnormalities should be weighed against the risk to the foetus of untreated maternal hypothyroidism. Liothyronine is contraindicated in pregnancy. Discuss with specialist endocrinology team.

Breastfeeding:

- An increase in monitoring of thyroid function tests may be required, discuss with specialist endocrinology team.

13. Specialist contact information

Back to top

Sheffield Teaching Hospitals

Name: Dr Amit Allahbadia

Role and specialty: Consultant Endocrinologist

Daytime telephone number: 01142434343

Routine referrals: please refer via ERS.

Alternative contact:

Out of hours contact details: *Sheffield Teaching Hospitals NHS Foundation Trust switchboard – Endocrinologist on call.*

Barnsley Hospital NHS Foundation Trust

Name: Dr Z Merza

Role and specialty: Consultant Physician & Endocrinologist

Daytime telephone number: 01226 730000

Routine referrals: please refer via ERS.

Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust

Name: Dr Shivani Dewan

Role and specialty: Consultant Endocrinologist

Daytime telephone number: 01302 366666

Routine referrals: please refer via ERS.

The Rotherham NHS Foundation Trust

Name: Dr Kavita Kulavarasalingam

Role and specialty: Consultant Endocrinologist

Daytime telephone number: 01709 820000

Routine referrals: please refer via ERS.

14. Additional information

Back to top

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

15. References

Back to top

1. NICE NG145: Thyroid disease: assessment and management. Last updated October 2023. https://www.nice.org.uk/guidance/ng145
2. Ahluwalia R, Baldeweg SE, Boelaert K, et al. Use of liothyronine (T3) in hypothyroidism: Joint British Thyroid Association/Society for endocrinology consensus statement. Clinical Endocrinology 2023; 99 (2): 206-216. https://onlinelibrary.wiley.com/doi/full/10.1111/cen.14935
3. Morningside Healthcare Ltd: Summary of Product Characteristics. Liothyronine Sodium BP 20 micrograms Tablets. Accessed via https://emc.medicines.org.uk/medicine /
4. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press

16. Other relevant national guidance

Back to top

1. NHS England. Liothyronine—advice for prescribers. August 2023. https://www.england.nhs.uk/long-read/liothyronine-advice-for-prescribers/
2. NHS England. Items which should not be routinely prescribed in primary care: policy guidance. August 2023. https://www.england.nhs.uk/long-read/items-which-should-not-routinely-be-prescribed-in-primary-care-policy-guidance/#appendix-further-detail-for-each-item
3. NHSE policy – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
4. General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care

5. NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

17. Local arrangements for referral

Back to top

Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

Liothyronine alone or co-prescribed with levothyroxine will be initiated and optimised in secondary care. Only once the patient is optimised with no anticipated further changes expected in the immediate future will prescribing be transferred to primary care. Monitoring will take place in secondary care and primary care will be informed of any dose changes.

Appendix 1: Some possible causes of persistent symptoms in euthyroid patients:

Endocrine / autoimmune	Diabetes mellitus Adrenal insufficiency Hypopituitarism Coeliac disease Pernicious anaemia
Haematological	Anaemia Multiple myeloma
End organ damage	Chronic liver disease Chronic kidney disease Congestive cardiac failure
Nutritional	Deficiency of any of the following: Vitamin B12, folate, vitamin D, iron
Metabolic	Obesity Hypercalcaemia Electrolyte imbalance
Drugs	Beta-blockers Statins Opiates
Lifestyle	Stressful life events Poor sleep pattern Work-related exhaustion Alcohol excess
Other	Obstructive sleep apnoea Viral and post-viral syndromes Chronic fatigue syndrome Carbon monoxide poisoning Depression and anxiety Polymyalgia rheumatica Fibromyalgia long covid

Appendix 2: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*:* *[insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed SY *IMOC* shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care, and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber /and Patient have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you are in agreement, please undertake treatment from *[insert date]* NB: date must be at least 3 months from initiation of treatment.

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days of receipt.

Appendix 3: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will provide ongoing monthly prescriptions as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp:

Appendix 4: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re*:*
Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS**,** in conjunction with local acute trusts have classified *[insert medicine name]* as a Shared Care drug and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patient's primary care prescriber, I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
3.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	

4.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed***.*** For this reason, I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
5.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp: