

19th October 2017

Submission from Thyroid UK in respect of NHS England Consultation “Items which should not be routinely prescribed in primary care: A Consultation on guidance for CCGs”

Due to the complexity of our response Thyroid UK is submitting its response in the form of a written submission rather than use the online form.

Introduction to the issue regarding liothyronine (T3):

Thyroid UK is a charitable company that provides information and resources to promote effective diagnosis and appropriate treatment for people with thyroid disorders in the UK.

Since its inception, Thyroid UK has come to realise that a large sub group of patients do not do very well on the standard treatment for hypothyroidism – levothyroxine (T4). Recent research shows that the sub group is 10-15% of patients and, in fact, we believe that the true figure is much higher than that due to the fact that many patients are self-treating with T3 which means that the data used for research is incorrect.

Up until 2015 more and more GPs and endocrinologists were realising that some patients did far better with the addition of T3 but unfortunately, in 2015 things changed.

In 2015, PrescQIPP published two bulletins – Bulletin 117 - The PrescQIPP DROP-List 2015 (Drugs to Review for Optimised Prescribing)¹ and Bulletin 121 - Switching liothyronine (L-T3) to levothyroxine (L-T4) in the management of primary hypothyroidism² which showed how much the price of T3 had increased. Along with the bulletins they published a template letter explaining how doctors can switch their patients from combination of T4 and T3 to T4 only.

PrescQIPP made an error in their initial bulletin regarding hypothyroidism guidelines and no thyroid patient groups were invited to take part in any discussions prior to the publish of this document.

The main subscribers of PrescQIPP are Clinical Commissioning Groups (CCGs) and once these documents were published we noticed a trend of CCGs refusing to allow doctors to prescribe T3 for their patients and also recommending that doctors switch any patients on T4/T3 combination treatment to T4 only treatment.

We are aware that some CCGs, however, are continuing to allow the prescribing of T3 to patients and we believe that this “postcode lottery” effect has now led to the NHS England Consultation “**Items which should not be routinely prescribed in primary care: A Consultation on guidance for CCGs**”.

Thyroid UK's submission:

On behalf of all thyroid patients in the UK, Thyroid UK strongly disagrees with the deprescribing of liothyronine for all patients.

Introduction

In what capacity are you responding?

Patient Representative Organisation

Name? (Optional)

Lyn Mynott, CEO, Thyroid UK

Email address? (Optional)

lyn.mynott@thyroiduk.org

Have you read the document 'Items which should not be routinely prescribed in primary care: A Consultation on guidance for CCGs'?

Yes

Equality and Health Inequalities

Do you feel there are any groups, protected by the Equality Act 2010, likely to be disproportionately affected by this work?

Sex

Age

Please provide further information on why you think this might be the case.

We feel that women would be disproportionately affected because the incidence of thyroid disease for women is 2% and for men 0.2%.³

On top of this, 87.5% of people who are prescribed liothyronine are women.⁴

Also, hypothyroidism mostly affects women over the age of 60.⁵

Therefore, the removal of liothyronine treatment would discriminate against women and women over the age of 60.

Equality and Health Inequalities – continued

Do you feel there is any further evidence we should consider in our proposals on the potential impact on health inequalities experience by certain groups e.g. people on low incomes; people from BME communities?

Yes

Please provide further information on why you think this might be the case.

Due to the high cost of liothyronine, caused by the Department of Health not intervening quickly when the manufacturers started increasing the price, if liothyronine is deprescribed, patients will need to find a way to source this medicine themselves. This will affect everyone who has been deprescribed, not just those on low income or who those who are not working although, obviously those on low income or not working will be affected much more severely.

Since some Clinical Commissioning Groups (CCGs) have already taken it upon themselves to deprescribe liothyronine, we already know that patients are having to obtain their liothyronine in different ways.

Some patients are being given private prescriptions by their clinician (on the advice of some NHS organisations).⁶

For some patients this means that their NHS clinician is providing the private prescription free of charge (which incidentally shows that the clinician is willing to provide a private prescription but is not being allowed to provide an NHS prescription) but that they are having to purchase the drug themselves at a cost of £258 per month if they are only on one tablet per day. In many cases, it is more expensive than this either due to the fact that a mark-up is added by the pharmacist or the pharmacist can only access T3 through a wholesaler who adds on his mark-up.

If the GP is not willing to give a private prescription, matters are even worse because these patients are finding private doctors and therefore they have to pay their fees which can range anywhere between £150 to £500 per hour plus the cost of the private prescription plus the cost of the medicine as I have mentioned before.

Some patients are purchasing liothyronine from online pharmacies which has its own problems such as not receiving a good quality drug or, in fact, tablets that are not drugs at all.

Another option that patients are using is travelling to Europe to purchase liothyronine from local pharmacies – in some European countries, T3 can be purchased over the counter. Obviously, there are costs involved in travelling to Europe although liothyronine can be bought for mere pounds rather than the exorbitant cost of the UK T3.

All of these options are going against the ethos of the NHS Constitution:

2. Access to NHS services is based on clinical need, not an individual's ability to pay

NHS services are free of charge, except in limited circumstances sanctioned by Parliament.

Since this is already happening, we know that the situation for patients is going to get exponentially worse.

How will the guidance be updated and reviewed?

How do you feel about the proposed process for identification of items for possible addition to the guidance or indeed possible removal, from the guidance?

Disagree

If needed, please provide further information

We feel that not enough patients were involved in any of the discussions prior to local CCG consultations that have already taken place and where CCGs have already deprescribed T3.

It seems that patients were not involved in decisions regarding this consultation or, if they were, misleading information was used as we have found in various copy letters received from NHS hospital trusts, CCGs, MPs and doctors.

Therefore, Thyroid UK does not have any faith that patients will be involved in any future reviews of any medications especially liothyronine, should the consultation result in it being able to be prescribed again.

More patients should be involved in these decisions and the correct information should be given to those discussing these matters.

Proposals for CCG Commissioning Guidance

Do you want to provide views on the proposals for CCG commissioning guidance?

Yes

If you have selected 'Yes', please select which medication you would like to share your views on.

Liothyronine

Liothyronine

The following recommendations are proposed for Liothyronine, how do you feel about these recommendations?

Advise CCGs that prescribers in primary care should not initiate Liothyronine for any new patient.

Disagree

Advise CCGs to support prescribers in deprescribing Liothyronine in all patients and, where appropriate, ensure the availability of relevant services to facilitate this change.

Disagree

Advise CCGs that if, in exceptional circumstances, there is a clinical need for Liothyronine to be prescribed in primary care, this should be undertaken in a cooperation arrangement with a multi-disciplinary team and/or other healthcare professional.

Disagree

If needed, please provide further information.

Liothyronine, in this consultation, comes under the heading, “Items which are clinically effective but where more cost-effective products are available, including products that have been subject to excessive price inflation.” However, our submission includes aspects regarding statements about liothyronine not being clinically affective so that anyone involved in the decision about not deprescribing it, will be aware of the reasons it is clinically effective.

The Clinical Commission Groups (CCGs) are already informing GPs and endocrinologists not to prescribe liothyronine (T3) due to the cost of T3 which has risen from 16p per tablet to £9.22 per tablet over the past few years.⁷

On top of that, I have recently been informed that doctors are receiving incentives for reviewing all of their patients who are on T3 and have a target of switching 60% of these patients onto levothyroxine (Norwich CCG – 2016/17 Prescribing Quality and Savings Incentive Scheme Summary.)⁸ This is appalling.

There is some very misleading information being used by CCGs, GPs, endocrinologists, MPs and NHS hospitals. In copy letters we have received the wrong guidance is continually being quoted:

“It is worth nothing also that our guidelines follow the Royal College of Physicians guidance on the management and treatment of hypothyroidism which is also endorsed by Thyroid UK.”⁹

Not only did Thyroid UK **not** endorse these guidelines but the RCP guidance is outdated (2011) and has been superseded by the *“Management of Primary Hypothyroidism - Statement by the British Thyroid Association Executive Committee - Endorsed by the Association for Clinical Biochemistry and Laboratory Medicine, British Thyroid Foundation, Royal College of Physicians and the Society for Endocrinology”* published in the journal *Clinical Endocrinology* in 2015.¹⁰

In actual fact, the RCP guidance of 2011 actually states, *“(e) The RCP does not support the use of thyroid extracts or levothyroxine and T3 combinations without further validated research published in peer-reviewed journals. **Therefore, the inclusion of T3 in the treatment of hypothyroidism should be reserved for use by accredited endocrinologists in individual patients.**”*

This allows for patients who may require T3 to visit an endocrinologist to discuss whether the patient would be suitable for a trial of T3 treatment.

The later guidance by the BTA Executive Committee actually only addresses primary hypothyroidism. If a patient's body cannot convert T4 into the active hormone, T3, as it needs to do, this should be classed as secondary hypothyroidism because there is no problem with the thyroid gland itself. Since there is no guidance in respect of non-conversion of T3, doctors only have the BTA guidance to use and this is not sufficient.

The BTA guidance states, *“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.”* Note the word “routine”.

This indicates that not **every** patient should be prescribed T3. We are not asking that every patient is prescribed T3. We are asking that the 10-15% of patients who do not resolve all of their symptoms are given a trial of T3.

The guidance also states, “12. If a decision is made to embark on a trial of L-T4/L-T3 combination therapy in patients who have unambiguously not benefited from L-T4 then this should be reached following an open and balanced discussion of the uncertain benefits, likely risks of over-replacement and lack of long-term safety data. Such patients should be supervised by accredited endocrinologists with documentation of agreement after fully informed and understood discussion of the risks and potential adverse consequences.

*Many clinicians may not agree that a trial of LT4/ L-T3 combination therapy is warranted in these circumstances and their **clinical judgement must be recognised as being valid** given the current understanding of the science and evidence of the treatments (2/+00).”* (Emboldening my own)

This statement indicates that some patients can be given a trial of combination treatment as long as patients are seen by an endocrinologist.

Unfortunately, many patients have actually been refused a referral because their TSH and or FT4 test is normal. An FT3 test is needed to diagnose a T3 issue in a patient and therefore FT3 tests should become part of the thyroid function tests that the NHS undertake to diagnose patients.

The BTA has since issued further guidance in respect of the use of combination treatment in some patients for GPs, patients and endocrinologists, in response to CCGs and doctors withdrawing T3 from patients.¹¹ This guidance can be found here: <http://www.british-thyroid-association.org/current-bta-guidelines->

This seems to be being ignored by CCGs and clinicians.

From copy letters we have received, we would like to correct other erroneous statements;

“The variation in hormonal content and large amounts of liothyronine may lead to increased serum concentrations of T3 and subsequent symptoms of thyroid excess, e.g. palpitations and tremor. Over-replacement with any thyroid hormone (T3 or T4 alone and T4+T3) may be associated with osteoporosis and may increase the risk of atrial fibrillation.”

This statement is full of “may be’s”. It’s also possible that T3 *may not* cause these problems. Surely, if the patient is informed of these possibilities and is still willing to start a trial, it is the patient’s choice?

“Liothyronine is available as licensed (and unlicensed) 20 microgram tablets and unlicensed 5 microgram tablets. Many other liothyronine-containing preparations are also unlicensed. Therefore, the safety and quality of these products cannot be assured.”

Liothyronine manufactured and licensed in European countries is as safe as the liothyronine manufactured here otherwise the MHRA would not have allowed pharmacies to access these when there was a supply issue in respect of T3 a few years ago.

“The amount of active ingredient in the liothyronine products from different suppliers may not be standardized. Variability in control means that there is a batch-to-batch variation”

Liothyronine is manufactured under license from the MHRA and must contain “90.0 – 110.0% of the stated amount”.¹²

Levothyroxine is manufactured under license from the MHRA and must contain 90 – 105% of the stated amount. The document, also states, in respect of levothyroxine, *“This gives some allowance for the known instability of the formulated drug*

*substance and is considered clinically acceptable (i.e. variation within these limits is unlikely to have significant clinical effects)."*¹³

This document shows that there is going to be a very slight batch-to-batch variation in both liothyronine and levothyroxine. Why is it that doctors are only concerned about variation in T3 tablets and not levothyroxine?

There are organisations other than Thyroid UK who are not happy about the restrictions proposed in this consultation.

The BMA are also not happy¹⁴ about the fact that NHS England plan to stop prescribing drugs for patients:

"The BMA's GP committee recognises the need to prescribe in a cost-effective manner, but where prescribing is changed for any other reason than clinical benefit to the patient, the patient must be involved and the extra workload for GPs needs to be recognised. Any prescribing policy needs to include flexibility to allow GPs to continue to meet individual patient's needs without having to negotiate bureaucratic hurdles."

and

"GP's have a contractual duty to prescribe drugs that their patients need and pressure must not be placed on them to act in a way that may contravene those regulations."

Professor Azeem Majeed has stated in the British Medical Journal¹⁵ that, *"However, this locally based approach is flawed. Firstly, CCGs have no legal power to limit the prescribing of drugs by GPs. As CCG policies on restricting prescriptions are not backed by statutory guidance, the inevitable result will be variation between GPs in the use of the drugs that CCGs are proposing to restrict – thereby leading to 'postcode prescribing.'"*

CCGs have no legal power to enforce doctors to stop prescribing drugs yet CCGs seem to be making their own policies in this regard in a snowball effect. Professor Azeem has reported NHS Dudley CCG to the Advertising Standards Agency for misleading patients on over the counter prescribing, *"because 'CCGs have no legal right' to limit the drugs GPs can prescribe."*¹⁶ GPC clinical and prescribing policy lead Dr Andrew Green has warned that CCGs do not have the power to ban GPs prescribing medicines that patients need. He told GPonline, *"If faced with upsetting their CCG or complying with GMS [General Medical Services] requirements GPs 'should upset their CCG every time.'*¹⁷

Thyroid UK believes that the savings that the CCGs want to make by refusing to prescribe T3 is a false economy because patients who are ill on levothyroxine will simply be returning to their clinician/GP/endocrinologist with their symptoms and find themselves going on a merry-go-round of specialists to find a cause of their symptoms. This will cost the NHS much more money than they will be saving.

Thyroid UK would like NHS England to be aware of the following:

Levothyroxine is **not** an alternative to T3. It is a **separate** hormone completely. The thyroid gland produces 80% T4 **and** 20% T3. If a patient has had a total thyroidectomy, they are immediately missing 20% of the active hormone. Giving these patients levothyroxine only, will **not** mean that they will convert their T4 into enough T3 for their bodies' cells.

Also, some people have a polymorphism that causes poor conversion.^{18, 19, 20}

Recent research has found that hypothyroid patients on levothyroxine had lower levels of T3 than healthy individuals (poor converters) and were heavier and differed in other objective and subjective measures. Some patients clearly did not convert at the same rate as others. **Everyone is not the same.**^{21, 22, 23, 24, 25, 26, 27, 28, 29, 30,31}

10-15% of all hypothyroid patients taking levothyroxine have impaired quality of life despite normal TSH concentrations. Could impaired conversion of thyroxine to T3 be the reason for this?³³

Research shows that long term use of T3 is safe.^{33, 34}

Studies investigating the efficacy of T3 substitution (liothyronine) gave varying results. However, some patients found improved quality of life under substitution therapy with T3 and preferred the combination treatment.^{35, 36, 37, 38, 39}

More and more doctors are realising that levothyroxine alone is not sufficient for many patients. Patients in many of the studies much preferred combination treatment and it was associated with improved metabolic profiles.^{40, 41, 42, 43, 44, 45, 46, 47, 48,49} How much more research do we need before patients are tested properly to see if they need T3 and then given T3 treatment?⁵⁰

It's not just the thyroid that is affected by low T3 – many patients may have hidden low T3 syndrome. Research has shown that low fT3 was the most important predictor of cumulative death. Also, depression is shown to be caused by low T3 levels. If FT3 testing is not done, many patients could suffer unnecessarily.^{51, 52, 53, 54, 55}

Recent research is being ignored^{56, 57, 58, 59} and the guidelines used by clinicians need to be updated, particularly the UK Guidelines for the Use of Thyroid Function Tests 2006⁶⁰ as these were meant to be reviewed in 2009 and Healthcare Improvements Scotland state in their Scoping Report dated 22nd February 2014⁶¹ that “UK guidelines for the use of thyroid function tests published in 2006 were based on a nonsystematic review of generally poor quality evidence from the United States (US) National Academy of Clinical Biochemistry (now archived).”

In regard to the fact that these guidelines are out of date, Miss Ashley Shalloe, Administrator, Association for Clinical Biochemistry and Laboratory Medicine has stated that, “The issue of maintenance and review of documents hosted on the ACB

website was discussed at the Scientific Committee meeting on 1st September, and a decision was taken to escalate a recommendation to the Executive Committee.

The specific document was prepared by people who are mostly not now professionally active, so it is thought that it is unlikely to be updated. It may be removed or it may be kept on the website with a clear indication that it is now out of date and unlikely to be updated.

The minutes of committee meetings such as that on 1st September are for internal use only and not publicly available.” and we await further news as to whether these will, in fact, be updated.

Doctors need to be aware that T3 testing is important in the **treatment** of hypothyroidism and not dismiss patients’ concerns, especially since the research referenced in the following paper (*Patients’ attitudes and perceptions towards treatment of hypothyroidism in general practice: an in-depth qualitative interview study by Rosie Dew, PhD et al in the BJGP journal - <http://bjgpopen.org/content/bjgpopen/early/2017/06/26/bjgpopen17X100977.full.pdf>*) is out of date:

“Patients that felt unwell also believed that TSH levels were too crude a measure to gauge *optimal thyroid hormone replacement. Some more informed patients had approached their GP and asked for further tests to check their triiodothyronine (T3) and thyroxine (T4) readings, as they felt unwell and dissatisfied with their treatment. However, since T3 measurements have limited value in the management of hypothyroidism*⁶² *these tests are not routinely offered.*” (32. Carter JN, Corcoran JM, Eastman CJ, et al. *Effect of severe, chronic, illness on thyroid function. The Lancet - 1974; 304(7887): 971–974. doi: 10.1016/S0140-6736(74)9207*)

In much of the copy correspondence I have received, there is the statement, “*I should clarify that decisions about what medicines to prescribe are made by the doctor or healthcare professional responsible for that part of the patient’s care and should not be made based entirely on the cost of the medicine. The cost of a medicine has to be balanced against the importance of meeting the individual treatment needs of patients and potential additional costs to the NHS if supply is interrupted.*”

Thyroid UK believes that the person who should actually make the decision as to whether a patient should be prescribed T3 is the clinician dealing with the patient and, in fact, this was confirmed at the face to face meeting in London in regard to this consultation, on 5th September when Dr Graham Jackson, Co-Chair of NHSCC; Chair, NHS Aylesbury Vale CCG, categorically stated that doctors could decide for themselves whether to prescribe T3 for a patient who had a clinical need.

Will Quince MP responded to his constituent with the statement, “However, clinicians are not prevented from considering other forms of thyroid hormone replacement, if appropriate.”

NHS England also state that, “*The proposed guidance would not remove the clinical discretion of the prescriber in deciding what is in accordance with their professional duties.*”⁶³ It is very clear to Thyroid UK that this statement is being completely ignored by CCGs who have been running their own consultations and making their own decisions about the stopping of T3 to patients. Many CCGs are not reinstating patients’ prescriptions of T3 even though the doctor has completed an Individual Funding Request (IFR).

In my experience, however, doctors are actually having their choice of treatment for a patient taken away from them. They are being forced to switch their patient from T3 to levothyroxine against both their own wishes and those of the patient. We are hearing that many doctors are informing their patients that they do not wish to switch their patient to levothyroxine but that they have no choice.

The doctor must have the overall responsibility and decision making about a patient’s treatment. The CCGs do not know the patient and what their needs are. **Patients’ needs should come before cost.**

The Concordia generic T3 is astronomically expensive at £854 for 100 20mcg tablets. There are far cheaper alternatives to the UK brands of T3 in Europe - in Germany the cost is £25.46 (30.15 Euro) for 100 tablets and in France it is a mere £9.83 (11.60 Euro) for 100 tablets. A few years ago, when there was a supply issue in regard to T3, pharmacies were able to access it from outside of the UK.⁶⁴

If pharmacies were able to do this now, it would mean that the NSH would save a huge amount of money and patients would be served well too. For the future, it would be a good idea if the NHS looked at their procurement system and made changes that automatically allowed pharmacies to use medicines outside of the UK if the UK generics/brands were too expensive.

We are aware that the Competition and Markets Authority (CMA) are investigating Concordia in respect of their conduct in respect of anti-competitive behaviour - <https://www.gov.uk/cma-cases/pharmaceuticals-suspected-anti-competitive-agreements-and-conduct> Morningside Healthcare have now started manufacturing their brand of T3 at approximately 50p cheaper than the Concordia brand. Hopefully, this will be investigated too.

The CMA have been looking at the issues with regard to Concordia and the price of liothyronine for many months. NHS England must have been aware of this and should have delayed this consultation until the investigation was completed.

If NHS England was not aware of this investigation, then I think communications between NHS England and the Department of Health are lacking.

Finally, we would like to make the following comments:

The fact that a subgroup of patients feel so much better on T3 and have been for better for many years shows that T3 should not be deprescribed for patients already

taking the drug (that is unethical) and should continue to be prescribed to patients who are only just finding out that they can feel better than they do on levothyroxine.

The NHS Constitution states, *“You have the right to receive care and treatment that is appropriate to you, meets your needs and reflects your preferences.”*

The main problem here is that a pharmaceutical company has been allowed to increase the cost of T3 without the Department of Health intervening until it was too late.

Please don't make patients suffer due to something beyond their control.

Items that are prescribed in primary care and are available over the counter

Please provide your views and/or any relevant evidence that we should consider when developing proposals to potentially restrict items that are available over the counter.

We believe that a doctor should be allowed to make a decision regarding any treatment he wants to prescribe for a patient including whether or not that particular patient can afford to pay for the drug over the counter.

Many people who are on benefits or on pensions cannot afford to pay for drugs they need for their condition especially elderly patients needing pain killing drugs.

Do you agree with our proposed criteria to assess items for potential restriction?

Neither Agree nor Disagree

If needed, please provide further information.

The criteria are sufficient. However, when NHS England research the separate criteria, they need to be certain that they have the correct information and to take into account patients' preferences especially since side effects are very subjective.

Everyone is different and different people may suffer different side effects on different drugs.

Just because an alternative drug is available, it does not mean it is suitable for the patient.

If a drug prescribed on the NHS is expensive and the NHS want to save money, the drug tariff system and the procurement system needs to be looked at before deprescribing a much-needed drug. Cheaper options need to be found even if this means accessing drugs from outside of the UK.

One more point I would like to make is that this consultation does not seem to have been circulated very well to patients by NHS England.

Thyroid UK sent an email to all of our members this week and, not only did the system crash for many of them but this was the first time they knew about the whole consultation. NHS England should ensure that all GPs send out a notification to all of their patients. This should not be difficult in this age of technology in the NHS.

My concern is that many patients have no idea about this consultation and will be upset that they were not able to contribute their views.

We sincerely hope that NHS England listen to patients in respect of deprescribing liothyronine as if you don't listen, this is going to affect thousands of patients' lives.

**Are there individual products, which are either clinically ineffective or available over the counter which you believe should be prioritised for early review?
Please give detailed reasons for your response.**

The re-prescribing of liothyronine needs to have an early review due to the fact that many CCGs have already deprescribed this drug.

About you

Not applicable

References below:

Research:

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