

PE1463/OOOO

Elaine Smith MSP submission of 14 September 2017

During the consideration of the petition on thyroid diagnosis and treatment over the past 5 years, I had thought that the issue of T3 (Liothyronine) was moving forward due to the positive experience of patients and the research. However, worryingly this has now gone backwards and I am keen to share the information I have with the committee.

The following is a summary of correspondence I have sent and received to date regarding the issue of liothyronine (T3) being withdrawn as a treatment for thyroid patients by NHS Lanarkshire as well as other health boards. The full correspondence has been attached as **Appendix 3**.

I was informed that this was the case in late 2016 by other patients in the region and sought to investigate it with relevant authorities, groups and individuals in order to ascertain if this was correct.

As the committee know, Hypothyroidism is a chronic illness affecting patients, over 90% of whom are women. The illness affects their whole health and wellbeing, and their ability to function in daily life including their ability to work.

Without access to T3 patients will be forced to either deteriorate or to self-medicate with costly alternatives being bought from abroad via the internet, which of course poses a serious health risk.

I also have serious concerns about the evidence and references used to reach this decision and have set out the details of that in this summary.

7th December 2016 Contact with NHS Lanarkshire

I wrote to the Chief Executive of NHS Lanarkshire stating that it had been brought to my attention that instructions may have been issued that liothyronine should not be prescribed due to high costs.

I noted that T3 is the only medicine available to patients suffering from Hypothyroidism who have a conversion failure when using T4 (levothyroxine) or who continue to suffer symptoms of hypothyroidism.

I described the petition which is currently going through the Scottish Parliament and included quotes from patients such as *"being prescribed T3 has given them their lives back"*.

I stated that I appreciate that in the UK Mercury Pharma have a monopoly over liothyronine and can charge NHS inflated prices, and the price of the drug in the UK is significantly higher than other countries, such as Germany and Sweden.

I asked for comments on this issue and a copy of any instruction that has been issued regarding the prescribing of T3.

6th January 2017 response from NHS Lanarkshire

In a letter sent by Callum Campbell, the Chief Executive of NHS Lanarkshire on 6th January 2017 I received the following assurance:

'I can advise you that NHS Lanarkshire has not issued any instructions about the use of liothyronine.

A group of NHS Lanarkshire clinicians are currently developing a clinical pathway for the use of the drug, including advice on appropriate prescribing. This guidance will be taken through NHS Lanarkshire's governance procedures before being accepted for use.'

I am currently pursuing an FOI to ascertain whether GP practices did in fact receive an instruction in 2016 to stop prescribing T3.

17th January 2017 Letter to NHS Lanarkshire

In a response letter to Callum Campbell, dated 17th January 2017, I explained that T3 is the only medicine currently available in the UK that can be prescribed to patients with hypothyroidism who do not do well on T4 or have a conversion failure. This has led to patients who experience this problem buying desiccated thyroid hormone on the internet from the USA or other countries, which is currently unlicensed in the UK.

In the UK Mercury Pharma (Concordia International) have a monopoly over the manufacturing and supply of T3, thereby holding the NHS to ransom by charging inflated prices for something available at significantly lower prices abroad. This leads to people experiencing symptoms such as depression, chronic fatigue, and fibromyalgia. In having to treat those symptoms the cost to the NHS in the long run is much greater than if they dealt with the problem at the source by prescribing T3 or DTH..

I also requested that a consultation be undertaken before deciding on the clinical pathway. I asked that any guidance be forwarded to me and information on whether the use of desiccated thyroid hormone would be considered, which would be a much more cost effective option for the many patients not doing well on T4.

This letter was copied and sent to the petitions committee previously.

27th February evidence to the Petitions Committee

On 27th February I gave written evidence to the public petitions committee of this Parliament regarding this issue.

5th July 2017 Letter from NHS Lanarkshire

On 5th July 2017 NHS Lanarkshire forwarded clinical guidance in relation to T3 and T4 which had been approved by the Lanarkshire Area Drug and Therapeutics Committee.

NHS Lanarkshire stated that this clinical guideline was in line with the cabinet secretary for Health's response to my question regarding liothyronine from 25 January 2017 which was as follows:

The decisions by endocrinologists on whether or not to prescribe a particular therapeutic is entirely a matter for that clinician, based on an assessment they have made of the patient's condition and the benefits and expected outcomes of prescribing a particular drug for that patient.

It should be highlighted that there is currently insufficient clinical evidence of the clinical and cost effectiveness to support the use of liothyronine (either alone or in combination) for the treatment of hypothyroidism. Thyroxine replacement therapy is essential in the treatment of hypothyroidism, with this usually being prescribed as levothyroxine

The guideline states that NHS Lanarkshire '**will not recommend the prescribing of liothyronine or liothyronine containing products for the treatment of primary hypothyroidism**' and '**do recommend prescribing of thyroid hormones in line with Royal College of Physicians guidance**'.

This is contradictory as the RCoP do support its prescribing by endocrinologists for individual patients.

The stated rationale and exceptions for this are attached in **Appendix 1**

Royal College of Physicians (RCoP) and British Thyroid Association guidance is attached in **Appendix 2**

28th August 2017 response to NHS Lanarkshire

In response to the letter of 5th July from Calum Campbell, NHS Lanarkshire, I wrote a further letter noting the comments in relation to the NHS guidance.

In particular, I noted that NHS Lanarkshire do not recommend prescribing T3 to treat hypothyroidism but do recommend prescribing thyroid hormones in line with the Royal College of Physicians (RCoP) guidance (Appendix 2).

I stated that I found this position to be inconsistent given RCoP recommend that the inclusion of T3 treatment should be allowed by endocrinologists. Furthermore, the Cabinet Secretary, Shona Robison, also confirmed that this decision should be made by an endocrinologist. I asked for further confirmation that endocrinologists will not be prevented from prescribing T3.

I then commented on NHS Lanarkshire's own guidance which was issued on the subject without any public consultation on the matter.

I specifically addressed the "Rationale" (Appendix 1) section of their letter with my own points as follows:

- The fact that thyroid treatment was changed in the 1980s to monotherapy does not make it the optimal treatment given there is current research to suggest combination therapy is superior.
- Many people in Scotland are successfully treated on T3 – this is indisputable
- Levothyroxine may be cost effective for health boards but at the cost of patients' health. It may not be suitable for many patients.
- Liothyronine can be taken throughout the day by halving the tablets to ensure steadier levels.
- If patients are not given the correct treatment, complications and additional problems, such as arterial fibrillation and osteoporosis may occur.
- The academic article by Dr Weirsinga et al that was cited by NHS Lanarkshire also suggests that combination therapy can be effective and NHS Lanarkshire have selectively quoted from the article.
- The fact that Concordia have a monopoly on supply and have been able to impose an unacceptable price hike is something that the medical establishment should be challenging instead of trying to remove lifesaving medicine from patients due to cost.
- NHS Lanarkshire's rationale that thyroid patients who are not effectively treated on T4 may have further problems not related to hypothyroidism, specifically mental ill-health, is unfounded and unacceptable. It also shows a lack of understanding that many patients cannot successfully convert T4.

I also considered the references used by NHS Lanarkshire and questioned many of these. I asked for comments on the evidence they gathered and particularly noted that they have been selectively quoting and using out of date research.

I followed by asking that NHS Lanarkshire confirm that GPs will be made aware of the fact that treatment should not be stopped or altered without a consultation from the patient's endocrinologist.

I concluded by asking if they could provide me with any correspondence they have had with Concordia, who own Mercury Pharma, to challenge their costing practice given the big price increase for T3 and confirm the names and occupations of those who were involved in the writing of the guidance.

CORRESPONDENCE TO, FROM AND IN RELATION TO MERCURY PHARMA

10th July 2017 letter to Concordia International

I wrote to Mercury Pharma (Concordia International) regarding the availability and cost of T3 given that their company is the sole manufacturer of the drug. I confirmed that T3 is the only licensed medicine available in the UK to patients who have a conversion failure or who continue to suffer symptoms despite T4 treatment.

I asked why the T3 drug was priced so highly and why Mercury Pharma charged the NHS inflated prices for it. I pointed out that the price of buying 100 tablets in Germany and Sweden would be £25 but in the UK the price would be £854.

21st July 2017 Response from Concordia International

Concordia International responded to my correspondence stating that the UK Department of Health *“has visibility on the pricing of all”* their medicines and *“has the ability to intervene on the pricing of any generic medicine where it feels the NHS is not receiving value for money”*.

28th August 2017 additional letter to Concordia

I sent an additional letter to Concordia International having discovered that local pharmacists are finding it difficult to source a supply of T3 at the moment.

I noted that I understand that there are only tablets with a use-by date of the end of October available at the moment.

I asked for clarification on the matter and to confirm whether there is a production problem with the drug.

29th August 2017 letter to DOH

I wrote to the UK Department of Health in light of the response from Concordia International, detailing the high cost of T3 in the UK in comparison to other countries and stated that Mercury Pharma appear to have a monopoly over the drug which allows them to charge an exorbitant amount.

I asked for their comments on the matter and highlighted the fact that Concordia International state that the Department of Health are entitled to intervene on such high prices.

29th August 2017 letter to Morningside Pharmaceuticals

I wrote to Morningside Pharmaceuticals Ltd to ask if they are currently supplying pharmacists in the UK with T3.

August/September 2017

A standard letter was issued by the ITT Campaign (Improve Thyroid Treatment) for members of the public to use when writing to their MPs and MSPs. It particularly references NHS England due to an on-going consultation, however the problem in Scotland is much the same.

The letter encourages constituents to share their own personal story and then provides a lengthy rationale of why Liothyronine is indispensable in the treatment of hypothyroidism.

On 11th September, I obtained a letter from NHS Scotland dated 24th August 2017 which had been circulated to the Scottish Prescribing Advisors Association, NHS Board Medical Directors and NHS Board Directors of Pharmacy. It states that NHS Scotland have “*identified an initiative which is unlikely to result in poorer patient outcome but is a cost effective opportunity to consider individual suitability to start/switch from liothyronine to levothyroxine capsules*”.

NHS Scotland make the point that levothyroxine has a longer life and provides suitable stable and physiological quantities of thyroid hormones. Liothyronine requires higher dosage than a single daily amount due to its life span. Slow release tablets do not seem to be available in the UK. It appears that NHS Scotland have decided that cost cutting, rather than a patient centred approach, is their primary objective.

Contrary to evidence stating otherwise, the letter concludes that combination T4+T3 treatment has not consistently been shown to be more beneficial than T4 alone.

Therefore, NHS Scotland are of the opinion that there should be a review process in which patients will undertake a consultation regarding their treatment with a view to moving them onto T4. Even if patients refuse this treatment, T4 will be offered to T3 patients as a trial, with the reassurance that returning to T3 will be possible at a later stage.

Given that T3 is experimental in itself as treatment, the fact that T4 is now being offered to T3 patients on an experimental basis seems inconsistent with the current approach and will result in patients being unwell. It appears that NHS Scotland are experimenting with the treatment patients are currently doing well on under the care of endocrinologists and failing to wait for the outcome of the petition currently at Committee.

Conclusion

I currently await responses from NHS Lanarkshire, NHS Forth Valley, Concordia International, the UK Department of Health and Morningside Pharmaceuticals. However, from the comments that I have already received it appears that there is a serious risk that prescribing of Liothyronine may be phased out, despite contrary evidence that combination or T3 therapy is effective.

NHS Lanarkshire are not in favour of the prescribing of T3 and it is concerning that this may be cut back further with the introduction of their trial as discussed in NHS Scotland's letter dated 24th August 2017 (see above).

It appears from the correspondence discussed above that cost can be considered a massive factor in determining the appropriate guidance for the prescribing of the drugs. However, T4 and T3 are not like-for-like drugs. This is not a case of effective substitution as there are many people who do not do well on T4.

Finally, I was recently made aware that Liothyronine is sometimes considered by the general public as a diet pill. A quick internet search can explain that Liothyronine increases metabolic rates and can increase weight loss. Perhaps the stigma

surrounding the drug as an illegitimate form of dieting is a catalyst for NHS Scotland to take steps to reduce its use despite the fact that it is being prescribed correctly and effectively by Endocrinologists for thyroid patients. This is completely unacceptable.

To conclude, T3 and T4 are very different medicines. T3 is the biologically active hormone ready to be utilised by the human body whilst T4 is a relatively inactive prohormone for which the body alone in the absence of T3 production from a working thyroid gland has to shoulder the extra burden of adequate conversion to T3. Therefore, T4 is neither an alternative nor a cheap substitute for T3 medication.

Appendices and Associated Documents

Appendix 1

NHS Lanarkshire Rationale

- Levothyroxine (T4) is a prodrug. It is converted to liothyronine (T3) in the body. Prior to the 1970s, synthetic combinations of levothyroxine and liothyronine or desiccated animal thyroid extracts containing varying amounts of thyroid hormones were used. These have now been replaced with the use of levothyroxine monotherapy.
- Levothyroxine is the thyroid hormone of choice.
- Levothyroxine is cost-effective, suitable for once daily dosing and provides stable and physiological quantities of thyroid hormones for patients requiring replacement (2).
- There is overwhelming evidence in support of the safety and effectiveness of levothyroxine alone in treatment of hypothyroidism.
- Liothyronine is not routinely recommended for prescribing as it has a much shorter half-life. Steady state levels cannot be maintained with once daily dosing. Multiple doses can lead to supraphysiological peaks and may not be able to avoid sub-therapeutic troughs.
- 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.
- There is currently insufficient clinical evidence of effectiveness and cost-effectiveness to support the use of liothyronine, either alone or in combination, for the treatment of hypothyroidism.
- Combination of levothyroxine and liothyronine, in both physiological and non-physiological proportions, has not been shown to be more beneficial than

levothyroxine monotherapy with respect to cognitive function, social functioning and wellbeing.

- 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.
- The amount of active ingredient in the liothyronine products from different suppliers may not be standardised. Variability in control means that there is batch-to-batch variation.
- It is recognised that some patients on levothyroxine remain symptomatic despite treatment. The reasons for this are poorly understood. Thyroid symptoms are nonspecific. Symptoms may be due to a non-thyroidal illness and/or may have a psychological dimension.

The exceptions in this case were as follows:

'1. Thyroid cancer patients: post thyroidectomy patients are required to take replacement hormone tablets for the rest of their lives. Patients that need to receive radioactive iodine treatment after their surgery will initially be started on liothyronine as it has a shorter half and a faster onset of action than levothyroxine making treatment easier. These patients will remain on liothyronine until the oncologist is confident that they will not need any more radioactive iodine at which point they are switched over to levothyroxine. This duration is usually two months up to six months until ablative radio-iodine treatment is complete.'

'2. Patients on levothyroxine who need Sestimibi scan for localizing parathyroid adenoma: The duration of treatment is between 4 and 6 weeks.'

Appendix 2

Royal College of Physicians and British Thyroid Association recommendation

- Patients with suspected primary hypothyroidism should only be diagnosed with blood tests including measurement of serum TSH.
- Patients with primary hypothyroidism should be treated with T4, using levothyroxine tablets (listed in the British National Formulary) alone.
- There is no indication for the prescription of levothyroxine or any preparation containing thyroid hormones to patients without an established diagnosis of thyroid disease and thyroid blood tests within the reference ranges.
- In patients with suspected primary hypothyroidism there is no indication for the prescribing of levothyroxine or any preparation containing thyroid hormones to patients with thyroid blood tests initially within the normal range. Thus patients with normal levels of T4 and TSH do not have primary hypothyroidism, and even if they

have symptoms which might suggest this, they should not be given thyroid hormone replacement therapy.

- The RCoP does not support the use of thyroid extracts or T4 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.

Primary Care Advice on Switching from Liothyronine (T3) to Levothyroxine (T4)

- In line with RCoP guidance, secondary care endocrinologists do not recommend routine prescribing of liothyronine and seldom initiate therapy of liothyronine on its own or in combination of liothyronine and levothyroxine.

- In exceptional situations, where T3 or T4+T3 therapy is initiated in secondary care, the rationale for treatment should be specified by the Endocrinologist. Treatment should not be stopped or altered in those patients without first consulting the secondary care specialist.

- For those who are on combination therapy without secondary care initiation, attempt should be made to convert to the appropriate equivalent dose of levothyroxine monotherapy in agreement with the patient.

- Face-to-face consultation with the General Practitioner or other clinician before conversion of therapy is recommended to avoid or minimise patient dissatisfaction.

- The patients should be made aware of non-specific nature of many thyroid complaints.

- Emphasis should be on the risks of non-physiological over-replacement.

- Consider reviewing the diagnosis and ensure that the patient is being treated for genuine hypothyroidism (i.e. confirmed biochemically in a test performed in an NHS accredited lab). If uncertain, stop the thyroid replacement and allow a rise in TSH in about 8-12 weeks.

- Switch from liothyronine (including liothyronine containing products) to the equivalent dose of levothyroxine. This should take into account any other levothyroxine that the patient is also co-prescribed if on combination therapy.

Appendix 3

See attachment entitled 'Appendix 3' containing the full correspondence.

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Correspondence with NHS Lanarkshire

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Pages 13-17, 28th August 2017 response to NHS Lanarkshire

Correspondence with and regarding Mercury Pharma (Concordia International)

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Pages 20-21, 21st July 2017 Response from Concordia International
Page 22, 28th August 2017 additional letter to Concordia
Page 23-24, 29th August 2017 letter to DOH
Page 25, 29th August 2017 letter to Morningside Pharmaceuticals
Pages 26-39, Suggested letter to political representatives