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Parliamentary Under-Secretary of State for Life Sciences
Department of Health
Richmond House
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27th March 2015

Dear George,

Further to our meeting yesterday, I am writing to set out to you clearly the failures on NHS England's part and hence the strong case there is for you to intervene and confirm the interim funding we are calling for.

Failure to have a robust, non-discriminatory process

The Health and Social Care Act 2012 scrapped the previous process for commissioning highly specialised treatments by disbanding the Advisory Group for National Specialised Services (AGNSS) in April 2013. This was a process that was supported by charities and families.

Fast forward to 29th October 2014, Dr Chris Hendriksz from Salford Royal Hospital sends an email to Ann Jarvis, who the day before chaired a meeting of a Programme of Care committee. Dr Hendriskz says "*Having had the time now to reflect on yesterday I just can not [sic] walk away without raising my multiple concerns*". He expresses strong concern about the scorecard system, evidence used for making decisions and the lack of documentation. He goes on to say "*I would suggest the scoring is not used at all for decision making this round*". Dr Hendriksz's full email is included in Appendix 1.

However the scorecard system is used nonetheless for recommending which drugs to fund. The recommendations were due to be approved at the 15th December 2014 meeting of the Clinical Priorities Advisory Group (CPAG). At the end of November[1], law firm Leigh Day submit a letter to NHS England threatening legal action that this process discriminates against those with ultra-rare diseases. The legal action was brought forward by Suzanne Mallah, mother of ten year-old

[1] http://www.leighday.co.uk/News/2014/November-2014/NHS-England-challenged-over-commissioning-procedur

Kamal Hoteit who has Morquio disease- one of only 88 people in the UK with the condition. A week later, NHS England scraps the process and announces it will start work to come up with a new process for commissioning treatments[2]. The 15th Dec CPAG meeting is cancelled.

At the end of January, NHS England launches a 90-day consultation, due to end 27th April, on the new process for deciding which treatments to prioritise for funding. During this nearly five month period, from the previous process being scrapped in early December until the end of April, there is no interim process in place, leaving patients with ultra-rare diseases and their families in significant uncertainty about future access to the drugs the patients need. And this is just those Morquio sufferers who were on the trial, ie. 34 of them. In other words, most of those with Morquio were not actually getting the drug, and this situation is a further significant delay to their getting access to Vimizim. Morquio is also a condition for which damage caused to one's body is irreversible- that is the cost of these delays. So when the Prime Minister, as he did on 11th March responding to me at Prime Minister's Questions, says "*I do not see any reason why there should not be continuity of care and continuity of drugs*", I am afraid to say he is excluding those who were not getting the drugs in the first place.

I am also concerned at a possible failure on NHS England's part to also learn from the above mistakes. In a presentation with stakeholders on Monday regarding the reason for the consultation, no mention was made of the legal challenge and instead the following sentence was used: "*a draft scorecard was tested but the Board decided in autumn 2014 was found to need further work*"! Further work was needed because NHS England put together a flawed process in the first place! I do hope NHS England are not trying to paper over this fact.

Failure to attend meetings

We have now met on 18th December and yesterday 26th March- NHS England have showed up to neither meeting. Only this Tuesday, 24th March, NHS England official Anthony Prudhoe told me directly that NHS England would be present at our meeting yesterday- yet they were not.

It is completely unacceptable for ministers to constantly claim this whole matter is for NHS England and then be unable to summon a NHS England representative to be answerable. It is also outrageous for an NHS England official to say he will be present at a meeting and then not be there.

Failure to reply to correspondence

Janis Clayton at PTC made a clear offer of a discounted price for Translarna to NHS England on a number of occasions, the first being on August 6th 2014, the most recent being February 6th 2015. She has had no official response from NHS England as to these communications.
Janis also further reviewed the budget impact with the responsible commissioner, Anthony Prudhoe. Anthony submitted the revised budget to Malcolm Qualie, Edmund Jessop and James Palmer on 13th March. When Janis followed up with Anthony on 24th March he still had not received any feedback.

On 9th October 2014, BioMarin also submitted a proposal to supply Vimizim to NHS England at a capped price over five years. They did not hear back despite repeated follow-ups. In a letter to James Palmer and Richard Jeavons, dated 28th February 2015, James Lennertz (Group Vice President and Managing Director of BioMarin Europe Ltd) says that *"due to no further discussions taking place between us and no action or agreement forthcoming from you, we are*

[2] http://www.leighday.co.uk/News/2014/December-2014/NHS-England-reveal-it-is-going-back-to-the-drawing

left with no option but to formally revoke the without prejudice offer made to NHS England" regarding supplying Vimizm. The offer had been made to Mr Malcolm Qualie. BioMarin will now cease to provide the drug for free from 12th May onwards.

My constituent Katy Brown, whose six year-old son Sam has Morquio disease, has strongly and very admirably campaigned hard for a secure, long-term arrangement for the treatment her son needs. Through her work with local media about Sam's case, she informs me that on 11th March, BBC Look North asked NHS England for a statement but two days later, there was still no statement. On Monday 16th March, Look North called up NHS England's press office, spoke to Tim Fernandez, who said NHS England would be making a statement later that day- no statement came but NHS England said there would be a statement the next day, but still nothing came. NHS England then said there would be a statement the following day- Weds, 18th March, yet nothing again. I understand that as of yesterday, BBC Look North still had not received the statement promised to them repeatedly by NHS England.

Aaron Revel and Paul Lenihan MBE, both from the Action Duchenne charity, recently wrote to Dr James Palmer, only to receive an acknowledgement reply saying *"Whilst I cannot guarantee a response…"* which is completely unacceptable. Again, if you say this is a matter for NHS England, they absolutely must be answerable and hence responding to queries raised with them. On this occasion, they received a reply after I emailed the relevant Case Officer demanding a response to Action Duchenne's correspondence.

Following our 18th December meeting at which you asked for early access research proposals to be sent in by PTC and BioMarin and both did so in January, you say in your 19th March letter to me that you referred these onto NHS England. However, neither company has heard back.

The above are just a few examples of NHS England's failure to reply- all of which merit further investigation about NHS England's willingness to be held accountable.

How NHS England have misled ministers

Your letter to me of 19th March says "*I can reassure you that NHS England is now in active discussion with BioMarin…*" NHS England are <u>not</u> in active discussion with the pharmaceutical companies – as Nigel Nicholls and Janis Clayton, of BioMarin and PTC respectively, made clear yesterday. NHS England have not tried to negotiate on price or even entered into a discussion for Vimizim or Translarna. Due to the lack of any timescales BioMarin have been forced to make plans to end compassionate use to those who were on the clinical trial. If NHS England had given firm dates and had communicated with BioMarin then the company would be able to provide treatment for longer enabling continuity of care. NHS England are being economical with the truth and need to be held to account.

Citing 'hung parliament' as an excuse

Both Jayne Spink (CEO of Tuberous Sclerosis Association) and Charlotte Roberts (Communications Officer of MPS Society) were present at yesterday's meeting. They both asked NHS England about specific dates for any relevant meetings after the consultation closes on 27th April. In response, they were told that there are no firm dates but that there will be a meeting in May/June on how a funding decision will be made and then a CPAG meeting will follow. However NHS England also said to them both that these rough timescales might be affected by a hung parliament. Again, if the entire issue is not a matter for ministers as you claim, why should

a hung parliament affect NHS England's decision-making processes? This is a serious matter which Bruce Keogh, James Palmer and Richard Jeavons must clarify.

No proper process in place

With respect to timescales, in addition to what Jayne and Charlotte mentioned above were told about a meeting in May/June, minutes of the 17th February meeting of the Specialised Services Stakeholder Surgery say:

> *"[Richard Jeavons] confirmed that the final decisions on what is prioritised would be made around June/July depending on meeting cycles following the end of the prioritisation consultation."*

May/June, June/July timelines are far too vague and not helpful. What is absolutely vital is that you set out clear, **specific** dates for when decisions will be made after the consultation closes on 27th April.

The lack of any timescales has also led to the unacceptable state of affairs where it is now 25 months since the Tuberous Sclerosis Complex funding bid was first presented to NHS England. In a case covered by the Health Service Journal this month, one patient, Julie Brooker died in January 2014 from a renal bleed caused by a tumour in her kidneys. Doctors had planned to treat her with Everolimus in August 2013, but Ms Brooker was unable to have the drug prescribed. Chris Kingswood, a consultant nephrologist who oversaw Ms Brooker's care, has said her death was "*absolutely preventable*" He is quoted in the HSJ article as saying: "*We know how effective the treatment is. With 95 per cent certainty we would have been able to successfully treat her and avoid the distress she had."* Another patient has already died this year, and a further patient's parents have been told to prepare for end-of-life care. Overall, 32 people need Everolimus, 15 of them face death, loss of their kidneys or risk of serious bleed. This is the cost of your and NHS England's delays and complete focus on bureaucracy rather than people's lives.

I will also repeat what BioMarin stated in their letter to you of 6th March:

> *'The EU legislation in the Transparency Directive clearly states pricing and reimbursement should be settled within one year of product approval."*
>
> *"In this case BioMarin has made every effort to achieve this with no decisions being forthcoming from [NHS England]. It should be noted that no other country which participated in the elosulfase alfa (Vimizim) Phase 3 Clinical Trial has even attempted to apply your interpretation of the Declaration or request or demand that BioMarin continue to supply free product."*

Secondly, as an extremely serious concern reflected unanimously by all the charities who were present yesterday, with respect to the consultation due to end on 27th April, there appears to be absolutely no methodology in place whatsoever and the consultation is on a "shell" process or "set of principals". As such it totally lacks substance and fails to demonstrate any thinking in relation to how decisions would actually be made. Without a methodology and definitions of terms how can NHS England make a decision about a technology or product one way or the other?

Given that NHSE has this far been unable to produce metrics, definitions or methodology whatsoever for assessing clinical effectiveness, value for money, cost effectiveness or safety (and

arguably the latter has been judged by the regulators in any case) or incorporating value of innovation. Ed Jessop and Fiona Marley confirmed that this was the case in a meeting with Stakeholders on Monday (attended by Jayne Spink and Charlotte Roberts).

There is no indication or published methodology for how NHS England will measure benefit to patients or how incremental benefits of new treatments will be taken into account.

There appears to have been no risk assessment / regulatory impact assessment undertaken for these policies.

NHS England say in their consultation document that it *"will only prioritise treatments or interventions where these can be offered to all patients within the same patient group".* If the patient group is defined as those with the condition rather than those who meet the licenced indication, Everolimus for TSC would be excluded. We don't know if this would be the case because NHS England have not defined the term "patient group".

NHS England say in their consultation document that they will only *"prioritise those treatments and interventions that demonstrate the greatest value for money"*. According to Ed Jessop and Fiona Marley (consultation stakeholder meeting) they have no intention of using the QALY as a measure and have no alternative methodology in place.

NHS England say in their consultation document that they will "*only commission for those prioritised treatments and interventions that are affordable within its relevant budget, and those that enable resources to be released for reinvestment."* This is utter nonsense and should not be used as a criterion for decision-making – is there an example of a new drug that has been "cost negative" at introduction (i.e. lowered a budget?). It would preclude introduction of "breakthrough" products and stifle innovation. There is also nothing in the document to define the term "relevant budget".

Furthermore, there are also mixed messages going out from NHS England. Action Duchenne were informed on 11th February, by Neil Churchill (Director of Patient Experience) that families would be able to receive interim access to Translarna via Individual Patient Funding Requests. However, a letter dated 24th March from Sir Bruce Keogh contradicts this statement. Action Duchenne were further told at a minuted meeting in February that Translarna would be included in an indicative budget for 2014/15, Sir Bruce Keogh's letter again contradicts this statement. I myself received a letter from Earl Howe, dated 11th December 2012, in which he says regarding my constituent Sam Brown, "*I can assure Mr and Mrs Brown that there are no plans to stop funding treatment for lysosomal storage disorders under the new arrangements for commissioning highly specialised services that will operate from April 2013."* I hope ministers do not contradict themselves and that Sam and his family can continue to rely on this assurance.

The case for ministers to intervene

Firstly, at yesterday's meeting, I quoted to you your Department's Framework Agreement with NHS England, which says, paragraph 4.11.13:

> *"If the Secretary of State considers that NHS England is significantly failing in its duties and functions he is able to intervene and issue directions to NHS England. This also applies where he or she considers NHS England has failed to act in the interests of the health service. In the first instance, the Secretary of State could direct NHS England about how it carried out its functions. If NHS England failed to comply with such*

directions, the Secretary of State could either discharge the function himself, or make arrangements for another body to do so on his behalf."

On Tuesday, the penultimate day for tabling Early Day Motions, I tabled EDM 918 making reference to the above and in that short time frame ten MPs have already added their names. 63 MPs had already signed EDM 819 as well, calling on you to put interim funding in place. If one of the key functions of a commissioning body is to have a robust commissioning process, I think we can safely conclude that NHS England is failing in this duty.

Secondly, Janis Clayton from PTC has helpfully also highlighted a further reason from the *NHS Commissioning Board (NHSCB) Commissioning Policy: Ethical framework for priority setting and resource allocation (Ref NHSCB/CP01)*, which says that the Secretary of Health can indeed decide that a healthcare intervention can be funded:

> ***Principle 9***
> *All NHS commissioned care should be provided as a result of a decision by the NHS CB. No other body or individual, other than those authorised to take decisions under the policies of the NHS CB, has a mandate to commit the NHS CB to fund any healthcare intervention unless directed to do so by the Secretary of State for Health.*

Thirdly, as I mentioned, in the NICE guidance HST1 'Eculizumab for treating atypical haemolytic uraemic syndrome' the following is stated "*The [NICE] Committee queried the reasoning behind NHS England's decision to commission eculizumab through an interim commissioning policy. It heard that there were potential irreversible implications for patients with aHUS if they did not have eculizumab treatment while waiting for the outcome of the NICE evaluation of eculizumab for aHUS.*" As this is clearly also the case for Morquio disease, Duchenne muscular dystrophy and tuberous sclerosis it would appear that precedent for intervening and providing interim funding is already set.

Lastly, with respect to your saying that you can only intervene if NHS England are not following their own processes, I would refer you to NHS England's Specialised Services Circular (SSC) issued 30th September 2013 and signed off by James Palmer and Kate Caston. The SSC is clear that, as of September 2013, interim policies should have been put in place. So we have had 18 months without perfectly possible interim policies, and with the NHS ignoring the provision for critical need prescribing. NHS England have been completely aware of this situation and taken absolutely no action to ensure their own policies were enacted. Which means that the avoidable deaths from TSC are directly related to a failure on the part of NHS England to invoke its own processes. Clearly, freeing up access does not create any unhelpful precedent - it merely follows NHS England's own policies.

So there is no reason why ministers cannot intervene and state that Translarna, Vimizim and Everolimus- all of which have clinical approval- should be funded from April 2015, the new NHS funding year. Meanwhile, I also ask whether Sir Hugh Taylor's review announced 11th March could play any role in an immediate solution.

Conclusion

I will finish by reiterating once again that we would not be in this situation if NHS England had not put forward a flawed and discriminatory process in the first place. The moral and potentially legal responsibility is therefore on them, and also on health ministers ultimately responsible for the NHS, to sort out this mess and put in place an interim process. We completely get the need

for a new process and are happy for you to consult away- but we need an interim process in the meantime.

Ministers must also stop hiding behind NHS England's bureaucracy and constantly saying this is a matter for them and not you. I have set out above NHS England's clear failings in being unwilling to respond to correspondence or even turn up to meetings despite giving me a face-to-face promise that they will do so. This is a completely unacceptable state of affairs. Even more so when you are clearly being misled, something for which Bruce Keogh, James Palmer and Richard Jeavons must be held to account and urgently so.

It is clear that the charities and drugs companies at yesterday's meeting have little faith in the ongoing processes, which they correctly say lack detail on methodology, metrics and specific timescales. The failures of NHS England throughout this matter have been significant, the case for ministers to intervene is strong and there is a clear basis for you to do so. I trust you will act without delay.

I await your urgent response to each of the points above.

Yours sincerely,

Greg Mulholland MP

Appendix 1: Email from Dr Chris Hendriksz to Ann Jarvis

From: chris hendriksz <cfya@sky.com>
Date: 29 October 2014 07:48:09 GMT
To: annjarvis@nhs.net
Cc: patroberts@savebabiesuk.org, iainmellis@nhs.net, john.walter@cmft.nhs.uk, "<Anita.Macdonald@bch.nhs.uk>" <Anita.Macdonald@bch.nhs.uk>
Subject: POC meeting feedback

Dear Ann

Please find the published papers as requested yesterday.

Having had the time now to reflect on yesterday I just can not walk away without raising my multiple concerns I have about the process I was part off yesterday. Irrespective of the decision I was deeply concerned about the bias towards the political agenda rather than patient care but maybe I was the only one who experienced it that way.

I did ask my question in the first session and never got a clear answer as to on what basis the weighting was based. I think when all our evidence is graded by Grade system and then to suggest that your weighting can be based on 6 sessions of focus groups is unacceptable. None of us on the table were aware of any of these focus groups so I am concerned if the voice of rare disorders was even considered. I think the evidence rating for the weighting should be provided and the same scrutiny and rules should apply meaning that unless this was obtained in a double blind RCT it should be excluded and not used or the principles of evidence should be the same for all.

The fact that we didn't have the documentation in advance speaks of poor practise and it is beyond my understanding how POC members are suppose to make decisions without having had the time to read the documentation.
Members of other POC groups have told me during lunch that the only received the policies the day before the meeting meaning no one will have had chance to read them. To then make decisions on a short presentation is deeply worrying. The guidance we were given before the meeting for presentation was unclear and i was under the understanding that the policy will at least have been read by members but I seriously doubt that.

Overall the evidence review which carries the most weight seemed to be shabby and not consistent and as this is to cover new developments it is clear that many papers will not be published within 18 months of completion of a trial so to insist on only peer reviewed papers again bias this to common disorders. Most people reported that the reviews were either out of date or no regards was given for non RCT evidence which contradicts the grading system.

I think the meeting also gave more time to some areas than others so it was not consistent through the day which would then make me question how the order of the day was decided. By the time we were giving evidence it was very short and rushed and voting fatigue was present.

I think the impact of rare diseases was poorly managed and glad that you will be taking this forward as the definition of a rare disease is clear.

The whole discussion and feedback about inequalities was farcical.

Sadly I must say in spite of all the caveats given at the start it can not accept that time pressure is an excuse for bad practise.

From a personal perspective I would suggest the scoring is not used at all for decision making this round and I would rather have people acknowledging that they are making random decisions than to try and given some credibility to a process that was deeply flawed.

Lastly my main concern is that everyone yesterday understood why we need to change and limitations of the process however by next year more than half of the decision makers will have moved on unless the NHS changes dramatically the incoming people will have no hand over and by next year we will be told a vigorous and fair system of scoring was trailed in 2014 and will now be used for the future and perpetuating bad practise in the NHS.

I am sorry if I missed some communication and for the record I am not a CRG member so may be less exposed to these meetings.

I am sorry to be so negative but my main responsibility is towards my patients and yesterday they were poorly represented and not fairly treated.

I said to some I felt like I was invited to play a game of Pointless but when I arrived I walked into the studio and was asked to play Family fortunes.

Chris Hendriksz
Clinical lead Adult Inherited Metabolic Disorders

Papers in PUBMED supporting my views and last one from 2012 predicting poor service for rare disorders as we change again:

1: Hendriksz CJ, Berger KI, Giugliani R, Harmatz P, Kampmann C, Mackenzie WG, Raiman J, Villarreal MS, Savarirayan R. International guidelines for the management and treatment of Morquio A syndrome. Am J Med Genet A. 2014 Oct 24. doi: 10.1002/ajmg.a.36833. [Epub ahead of print] PubMed PMID: 25346323.

2: Hendriksz CJ, Giugliani R, Harmatz P, Mengel E, Guffon N, Valayannopoulos V, Parini R, Hughes D, Pastores GM, Lau HA, Al-Sayed MD, Raiman J; STRIVE Investigators, Yang K, Mealiffe M, Haller C. Multi-domain impact of elosufase alfa in Morquio A syndrome in the pivotal phase III trial. Mol Genet Metab. 2014 Sep 6. pii: S1096-7192(14)00277-7. doi: 10.1016/j.ymgme.2014.08.012. [Epub ahead of print] PubMed PMID: 25284089.

3: Hendriksz CJ, Burton B, Fleming TR, Harmatz P, Hughes D, Jones SA, Lin SP, Mengel E, Scarpa M, Valayannopoulos V, Giugliani R; STRIVE Investigators, Slasor P, Lounsbury D, Dummer W. Efficacy and safety of enzyme replacement therapy with BMN 110 (elosulfase alfa) for Morquio A syndrome (mucopolysaccharidosis IVA): a phase 3 randomised placebo-controlled study. J Inherit Metab Dis. 2014

Nov;37(6):979-90. doi: 10.1007/s10545-014-9715-6. Epub 2014 May 9. PubMed PMID: 24810369.

4: Lavery C, Hendriksz C. Mortality in Patients with Morquio Syndrome A. JIMD Rep. 2014 Apr 10. [Epub ahead of print] PubMed PMID: 24718838.

5: Hendriksz CJ, Lavery C, Coker M, Ucar SK, Jain M, Bell L, Lampe C. Burden of disease in patients with Morquio A syndrome: results from an international patient-reported outcomes survey. Orphanet J Rare Dis. 2014 Mar 7;9:32. doi: 10.1186/1750-1172-9-32. PubMed PMID: 24602160; PubMed Central PMCID: PMC4016149.

6: Hendriksz CJ, Harmatz P, Beck M, Jones S, Wood T, Lachman R, Gravance CG, Orii T, Tomatsu S. Review of clinical presentation and diagnosis of mucopolysaccharidosis IVA. Mol Genet Metab. 2013 Sep-Oct;110(1-2):54-64. doi: 10.1016/j.ymgme.2013.04.002. Epub 2013 Apr 10. Review. PubMed PMID: 23665161; PubMed Central PMCID: PMC3755102.

7: Harmatz P, Mengel KE, Giugliani R, Valayannopoulos V, Lin SP, Parini R, Guffon N, Burton BK, Hendriksz CJ, Mitchell J, Martins A, Jones S, Guelbert N, Vellodi A, Hollak C, Slasor P, Decker C. The Morquio A Clinical Assessment Program: baseline results illustrating progressive, multisystemic clinical impairments in Morquio A subjects. Mol Genet Metab. 2013 May;109(1):54-61. doi: 10.1016/j.ymgme.2013.01.021. Epub 2013 Feb 9. PubMed PMID: 23452954.

8: Wood TC, Harvey K, Beck M, Burin MG, Chien YH, Church HJ, D'Almeida V, van Diggelen OP, Fietz M, Giugliani R, Harmatz P, Hawley SM, Hwu WL, Ketteridge D, Lukacs Z, Miller N, Pasquali M, Schenone A, Thompson JN, Tylee K, Yu C, Hendriksz CJ. Diagnosing mucopolysaccharidosis IVA. J Inherit Metab Dis. 2013 Mar;36(2):293-307. doi: 10.1007/s10545-013-9587-1. Epub 2013 Feb 1. PubMed PMID: 23371450; PubMed Central PMCID: PMC3590423.

9: Hendriksz CJ, Hughes DA, Mehta AB, Wraith JE, Jones SE, Ramaswami U, Deegan P,
Lachmann R, Murphy E, Hiwot T, Vijay SV, Stewart F, Cleary M. Transfer of high cost drugs to NICE risks fragmentation of care of rare diseases. BMJ. 2012 Aug 24;345:e5727. doi: 10.1136/bmj.e5727. PubMed PMID: 22923539.