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Dear Sirs

Single Technology Appraisal for Natalizumab for the treatment of Multiple Sclerosis – Appraisal Consultation Document

Thank you for your letter of 22 March 2007. I was very please to note that the committee concluded that Natalizumab was an effective treatment for relapsing remitting multiple sclerosis. However, I am disappointed with the outcome of the appraisal process and that the committee did not recommend using the treatment within the NHS.

As you may be aware I have made a formal complaint for amongst other things, the general treatment of patient experts and the fact that I did not feel that sufficient time was given for the meeting as the chairman made it clear that due to the late start of the meeting that we would need to speed through it. For your information, I have attached copies of my recent e-mail correspondence in respect of my formal complaint.

I do accept that there may be slightly differing agendas between patient experts and NICE in respect to the fact that NICE are more likely to want to remove the emotion from decision where as the patient expert will generally be keen to share some of their personal and emotional experiences of what it is really like to live with this very demanding disease. However, I really feel that the Committee missed a good opportunity to gain a greater understanding of MS and the effects on patients and their families, from the patient experts at the committee meeting. I believe that this would have helped clear up many of the points raised in this letter.

In response to your specific points I would say the following:

i) I do not consider that all the evidence was taken into account, as outlined in more detail below.
ii) I do not consider that the summaries of clinical and cost effectiveness are reasonable particularly when you are comparing Natalizumab with best supportive care which is not appropriate in this situation as in practice disease modifying therapies will generally always be used. I can therefore only conclude that this represents a complete misunderstanding of not only treatments of MS,

but the underlying disease and risks involved with not treating patients who have an active disease.

iii) There is a risk that a good opportunity to significantly reduce the number of relapses for patients with relapsing-remitting MS could be lost if the recommendations remain in their current draft form. It therefore follows that I do not consider that the provisional recommendations are sound and constitute a suitable basis for guidance for the NHS.

For ease of reference I have summarised my concerns with the document in the order that they arise:

1.1 – As mentioned above, I do not agree with your recommendation.

3.3 & 3.4 – I am please that you note that the AFFIRM study demonstrates that Natalizumab significantly reduces the probability of sustained disability progression. Furthermore it is noted that results showed that Natalizumab was associated with significant reductions in relapse rates when compared to other widely used disease modifying therapies. In view of the importance of these conclusions, I think that it merits highlighting these at the very start of document so that it is more obvious to the reader.

3.9 – I am concerned that the committee is making such a distinction between relapsing-remitting MS and highly active relapsing-remitting MS. I think that it is important to note that these are not two different types or diagnoses of the disease, they are merely labels that have been applied to peoples MS. An individual with highly active relapsing remitting MS has relapsing-remitting MS, but unfortunately, as the label suggests, their MS is particularly active as opposed to an individual that may be experiencing a lower number of relapses in a given period.

It therefore follows that if an individual is experiencing a larger number of relapses, ie they may be classed as having highly active MS over a particular period when compared to another patient, then it is of greater importance for them to have access to an effective disease modifying therapy such as Natalizumab, as the Committee have, as discussed above, concluded that Natalizumab is effective in reducing the number of relapses.

3.11 – I seem to recall that this point was discussed in the meeting, and it was stated that it was possible for patients to actually improve on this treatment. Consequently, I am not sure that the points raised here are entirely relevant.

4.4 & 4.5 – It is not appropriate to use best supportive care as a comparator for patients as it is simply inconceivable that patients with a very active MS would not take any disease modifying therapies.

Patients with active MS are very vulnerable to the damaging effects of this disease and it is therefore incredibly important to a patient's physical and mental health to ensure that they are actively taking steps to manage their disease. Otherwise it very quickly becomes a disease that manages them.

I do not therefore agree that this treatment should fail on cost effectiveness as the basis for the greater comparator in simply not an option.

4.6 – As above, I do not agree that best supportive care is an appropriate comparator. If it can be concluded that beta interferon are not as effective for this subgroup of patients, it surely strengthens the case for a need to have access to a drug such as Natalizumab that is effective in reducing relapses. It is not acceptable to simply ignore patients who have a highly active disease.

4.7 & 4.8 – For the reasons discussed above, I do not consider that these conclusions are sound. As currently drafted they demonstrate a complete misunderstanding of both the disease and the importance of having an effective therapy to reduce relapses, particularly when the disease is very active.

6.1 – As discussed above, we are not dealing with patients that have a different disease, it is the same disease that is more active than another individuals disease over a give period of time. I therefore do not understand the need for further clinical research.

Furthermore, the committee need to understand that patients who have a very active disease do not have time on their side with which to 'shop' around for treatments, to do so can lead to very damaging and disabling results. It therefore follows that if there is an effective treatment then patients with highly active disease should have the option of that treatment as soon as possible.

It is a very risky for patients such as my wife with very active MS to simply try differing range of treatments in the hope that they will manage the level of relapses, as each time a treatment is changed there is a risk that the MS 'rebounds' and causes severe relapses and untold damage, and may also be a risky period where no treatment is given. Therefore if we are looking to increase the level of a patient's independence and reduce the burden on the NHS it makes far more sense to offer a clinically effective treatment such as Natalizumab to such patients.

I also question the ethics of further research on patients with a very active disease as it is incredibly important for them to be on a disease modifying therapy.

Other points

I think that it is important for the Committee to understand that a relapse is not a specific event where it can be easily determined when it starts and ends, the lasting effects of a relapse can be very drawn out and very debilitating and consequently the long term costs to the NHS can be extensive. Whilst some of the symptoms may respond to steroid treatment or mend in time, the lasting effects can be very dramatic. It may take many months for the physical and mental health to recover, if in deed a full recovery is achieved.

Aside from the physical difficulties that this disease brings, the mental burden can be very significant. Therefore the importance of managing the disease and being in a position to try and control it goes well beyond the actual physical need. It therefore follows that it is of even greater importance for patients with very active disease to have an effective treatment available to them to help reduce the number of relapses.

My wife was diagnosed with MS in 1998. For the first six years my wife was largely well, but she experienced a very active stage of her MS when disease modifying therapy was stopped in 2004 as we were planning to start a family. As a result of this, my wife's physical and mental health has deteriorated rapidly, and the effects of MS on our family numerous:

- my wife is not able to do many things that a 'normal' mother would be able to do with their child such as holding our son or answering his cries,
- currently need full time care,
- not able to plan anything as little control of, or concept of what my wife's health will be at any point in time,
- base level of health is constantly changing, so therefore not able to try to adapt to disabilities as they are constantly changing, consequently the disease has the ability to trap us.
- our modest savings are currently being used to pay for childcare or personal care for my wife,
- reduction of cognitive ability and confidence, so we are not always able to make decisions as a family together.
- my role as a husband is constantly being eroded and removed to that of primary carer.
- I have not been able to work a full week in over a year, which brings both financial and physiological difficulties.

In addition to this, as a result of a very aggressive period in her MS, my wife is much more affected by infections as these tend to increase her body temperature and have a major impact has on her MS symptoms. This is a hidden cost of not effectively managing relapses and therefore the progress of the disease, and as a result of this, my wife has spent approximately three months out of the last five in hospital including a spell in intensive care. This further highlights the importance of the need to reduce the number and severity of relapses.

In summary, the Committee have concluded that this treatment is effective in reducing the relapse rates when compared to other widely used disease modifying therapies, and it reduces the probability of sustained disability progression. Consequently, I think that it is important that patients have access to this treatment on the NHS as the risks of severe reductions in both the physical and mental health of the patient and their family are so great, that an effective treatment is vital.

I look forward to seeing a revised draft of the recommendations. Please do not hesitate to contact me if you need any further information.

Yours sincerely

Mark Priest