Patient/carer group or patient expert statement

About you

Your name:

Name of your organisation (if applicable): Multiple Sclerosis Trust

Are you:
I am:

- an employee of a patient organisation that represents people with MS for which NICE is considering the technology
- My job title is: Director of Services
- In putting this submission together I have taken advice from:
  Chief Executive of MS Trust and person with MS
  Person with MS
  Person with MS
  Husband of person with MS
  Neurologist Royal London Hospital
  Neurologist Royal Victoria Hospital Newcastle

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition?

In order for NICE to effectively assess the advantages or disadvantages of natalizumab it is very important that they fully appreciate what a diagnosis of MS means to an individual, and in particular what it means to be one of the cohort of people who has highly active relapsing disease.

It is most likely that the individual would be given their diagnosis when young (25 – 35 years old) be in full-time work, and at a very important phase of their life with regard to personal relationships. The diagnosis of MS will ensure that for the rest of their life they will never again be able to plan reliably for the future.

MS is an unpredictable condition; from the outset patients will experience periods of relapse followed by remission. Research shows that on average a relapse lasts 55 days, or nearly two months. A person with MS is likely to have 2 – 3 relapses per two-year period, although for the highly active relapsing cases the relapses will be even more frequent and subsequent recovery significantly less. In essence this means that the person with MS is likely to have a minimum of 4 – 6 months of their life in a two-year period in relapse. This pattern of disease is totally disruptive to their family, leisure activities and importantly their career. In addition, for the highly active relapsing cases, recovery from relapses will be incomplete and thus the advance of

disability occurs early in the disease course. Premature retirement is a common outcome for the highly active relapsing cohort of patients.

It is very important that in assessing natalizumab, and in fact any disease modifying drug treatment, NICE now recognises the significant body of research evidence that has been gathered over the last decade which shows categorically that MS needs to be treated from the start. Once disability has set in, treatment is too late and for the person with MS the clock cannot be turned back.

Many research studies have shown that people with MS want to play an active part in "society" and not be a "burden". Pro-active early relapse management is the way to achieve this.

1. **Advantages of Natalizumab (Tysabri):**

Natalizumab is a welcome advance in the treatment of multiple sclerosis. In particular the advantages to the person with MS are:

- reduced disease progression
- reduced number and severity of relapses
- reduced administration of steroids
- fewer hospital admissions
- improved quality of life and reduced cognitive decline

1. Reduced disease progression:
At two years the cumulative probability of disease progression was 17% in the natalizumab group and 29% in the placebo group. Any reduction of disease progression is a significant benefit to prevent the onset of life-long dependence.

2. Reduced relapses:
Natalizumab has been shown to reduce the annualised rate of relapses by 68%. After one year 77% of patients on treatment were relapse free as compared to 56% in the placebo group. Over two years natalizumab reduced the risk of relapse by 59%. A reduction of the number of relapses will enable the person with MS to stay in work, to have a fuller family and social life.

3.Reduced administration of steroids:
Administration of steroids is undesirable but often essential for people with MS in relapse. In the Tysabri study 50% of patients on the placebo arm needed steroids but only 15% on the Tysabri arm. Reducing the use of steroids reduces the long-term effects of their usage and subsequent complications for example osteoporosis, diabetes etc.

4.Reduced hospital admissions:
People with MS are often hospitalised if their condition worsens and natalizumab has been shown to reduce the rate of hospitalisations by 65% over two years.

5. Improved quality of life and reduced cognitive decline:
In addition to the very tangible physical benefits quoted above natalizumab has also been shown to have a positive effect on quality of life for people with MS.

It is impossible to over-estimate the impact of a long-term condition such as MS. It is also impossible to under-estimate the positive impact of decisive action early in the disease course. This gives the individual back some control of their life as well as reducing the long-term risk of serious disability, and enabling the individual to stay in work, and have a full family and social life.

Work provides a structure to life and for a young person to lose their job not only reduces their earning potential and thus financial independence, it also minimises their role in society with all the inherent mental consequences. It is proven that people with MS have a much higher level of depression and suicide than the general population and lack of active management of their condition is a major contributor to the suicide risk.
The financial, personal and social impact of MS is very high.

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition? (continued)

2. **Disadvantages of natalizumab (Tysabri):**

The risk with natalizumab is the development of Progressive Multifocal Leukoencephalopathy (PML) and other opportunistic infections of the CNS. PML can be fatal if not diagnosed early and managed correctly. However the risk of PML must be put in context as discussed in the comparative section below.

People with MS will undoubtedly take the risk of PML seriously, but if one's disease is rapidly progressing one's assessment of risk will be different from someone with no disease. It is anticipated that specialist neurology centres will be administering natalizumab and thus risks of PML can be discussed with the person with MS and with effective monitoring they will be minimised.

3. **Are there differences in opinion between patients about the usefulness or otherwise of this technology? If so, please describe them.**

We are not aware of differences of opinion.

4. **Are there any groups of patients who might benefit more from the technology than others? Are there any groups of patients who might benefit less from the technology than others?**

In view of the safety considerations and the risk of PML the MS Trust is supportive of the licensing recommendations that natalizumab should be available to people with highly active disease:

- Patients with high disease activity despite treatment with a beta-interferon
- Patients with highly active relapsing relapsing-remitting multiple sclerosis

Comparing the technology with alternative available treatments or technologies

NICE is interested in your views on how the technology compares with existing treatments for this condition in the UK

(i) Please list any current standard practice (alternatives if any) used in the UK.

Natalizumab could be compared with the current beta-interferons and glatiramer acetate as the only other licensed products for the treatment of relapsing remitting multiple sclerosis and the data shows that natalizumab is more effective in reducing the number of relapses and thus the progression of disability.

The licence indication for natalizumab is for people with MS with high disease activity or severe relapsing remitting disease and for these people clinicians are currently using mitoxantrone off licence. This off licence usage carries significant risks for the clinician.

Mitoxantrone carries a 1:200 risk of cardiac problems for people with MS and a 1:400 risk of promyelocytic leukaemia. This compares with the 1;1,000 risk of PML with natalizumab.

The risk of PML will be acceptable to people with MS with high active relapsing disease, balanced against a better prognosis. Their alternative is a route to rapid disability.

For people with MS therefore it is a significant benefit to now have access to a therapy which has been appropriately assessed and has a license for treating severe relapsing remitting MS.

Finally, there is no safety data on using natalizumab after mitoxantrone. Would the side-effects be acceptable or would they be cumulative? This is not a risk that would be acceptable to people with MS.

(ii) **If you think that the new technology has any advantages for patients over other current standard practice, please describe them. Advantages might include:**

As stated above there are currently no other therapies that are licensed exclusively for the treatment of patients with highly active MS. Natalizumab therefore represents a new opportunity for people with MS, and this is a significant advantage.

Natalizumab is administered by intra-venous infusion on a monthly basis and this will be positive for people with MS. It will ensure that they can be monitored whilst they are having their monthly dosage, and it will also remove any responsibility for self-injection as required for the current disease modifying drug therapies. Natalizumab is well tolerated by patients, it is easy to administer and adherence will be high.

(iii) **If you think that the new technology has any disadvantages for patients compared with current standard practice, please describe them. Disadvantages might include:**

None

Research evidence on patient or carer views of the technology

If you are familiar with the evidence base for the technology, please comment on whether patients' experience of using the technology as part of their routine NHS care reflects that observed under clinical trial conditions.

To date we are not aware that there has been any prescribing on the NHS since the licence was granted. This lack of usage reflects the current financial constraints within the NHS rather than lack of clinical need. We are aware of a number of people with MS, who have been assessed by their clinician as appropriate for natalizumab, but who are not yet receiving the drug.
We have also had direct contact with people with MS who were on the original clinical trials, who were allowed to continue with the product at the end of the study but who were stopped from receiving natalizumab during the safety assessment review. Many of these have deteriorated significantly since stopping natalizumab, and now have significant disability.

Are there any adverse effects that were not apparent in the clinical trials but have come to light since, during routine NHS care?

No as far as we know.

Are you aware of any research carried out on patient or carer views of the condition or existing treatments that is relevant to an appraisal of this technology? If yes, please provide references to the relevant studies.

The US FDA safety investigation into natalizumab prompted the United States National MS Society to conduct a survey amongst people with MS to capture their views on availability of the drug versus risks. The full results can be found at the website shown below and this survey was part of the FDA review.
http://www.nationalmssociety.org/pdf/research/tysabrisurvey.pdf

Availability of this technology to patients in the NHS

What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

To have highly active relapsing multiple sclerosis is very distressing for the individual, their family and colleagues. It ensures a path to early disability, engenders a feeling of hopelessness and often leads to early death. For natalizumab to be made available on the NHS would provide a clinical choice for the neurologist, hope for the person with MS and also provide a feeling of control over the situation. Much has been made over the years about mental attitude for coping with disease. It is clear that a positive attitude can be very important and without natalizumab these patients whose disease is rapidly progressing are left without hope.

What implications would it have for patients and/or carers if the technology was not made available to patients on the NHS?

For natalizumab not to be available would once again put people with MS in the UK at a serious disadvantage when compared with Europe and the USA. It would leave people with MS who have highly active relapsing disease with only symptomatic options. This would ensure rapid progress of the condition and early disability. It would also question the work that has been put in by people with MS and neurologists to undertake the clinical trials for natalizumab that have granted it a European licence. In addition, patients currently enrolled in the natalizumab redosing safety study in England and Wales, would not have access to natalizumab at the end of the study. Finally untreated highly active relapsing MS results in repeated hospital admission for the person with MS.

Are there groups of patients that have difficulties using the technology?

We are not aware of any group of patients who will have difficulty with using natalizumab. The need to go to hospital for the infusion will be inconvenient for some people but when balanced against the potential benefits people with MS will undoubtedly be wiling to attend hospital.

Other Issues

Please include here any other issues you would like the Appraisal Committee to consider when appraising this technology.