Multiple Sclerosis Society

MS Society response to the NICE Appraisal Consultation Document (ACD) on Fingolimod

About the MS Society

Established in 1953 and with over 38,000 members and 290 branches, the MS Society is the UK's largest charity for people affected by multiple sclerosis (MS) and the largest not-for-profit funder of MS research in Europe. There are approximately 100,000 people with MS in the UK and, with 50 new people diagnosed every week, it is one of the most common neurological conditions affecting adults. We are committed to bringing high quality standards of health and social care within reach of everyone affected by MS.

Introduction

The MS Society is extremely disappointed with the draft recommendation not to provide Fingolimod on the NHS. Fingolimod has the potential to transform the lives of people with MS who fail to respond to injectable therapies. The MS Society believes that no person with MS for whom an effective treatment is available should be denied access to that treatment on the NHS, to do so would be both unethical and perverse

The decision not to recommend Fingolimod for the treatment of relapsing-remitting multiple sclerosis therefore needs to be reconsidered for the following reasons:

1. Evidence from people with MS

It is not clear how, and to what extent the MS Society's original written submission was considered in the formulation of the ACD. We did not, for example, witness discussion of the report during the committee meeting. We urge the appraisal committee to take into consideration and appropriately weight our written evidence, which encapsulates the views and experiences of over 1000 people with MS. There remain clear misconceptions relating to the impact of MS and, we would argue, a failure to understand the effect of relapses in a real life context.

Our survey has captured the reality of living with MS, including the impact of both the benefits and side effects of treatment in the longer term and more importantly, how these are viewed by people with MS. For example, in our survey, of those with experience of injectable disease modifying drugs (DMDs), 66 per cent reported having experienced flu-like symptoms (as opposed to 36.9 per cent in trials). Clinical

trials do not capture the real world impact of living with side-effects on a daily basis and the cumulative impact this can have over a number of years rather than months.

The patient representative giving oral evidence to the committee supported this written evidence. She stressed that whilst on Avonex, she lost two days out of every week due to the flu-like symptoms, whereas she had no side effects from Fingolimod. She explained that the side effects were not minor and if she had been left with no alternative other than Avonex, personally, she would have discontinued treatment. For her family there was a constant low level anxiety knowing that there will be another injection and another two days lost.

Another important factor that we feel is not given due weight in the ACD, is the physical and emotional impact of relapses. This treatment is significantly more effective at reducing relapses, periods when people with MS experience new neurological symptoms or when their old symptoms reoccur, than current first-line therapies. Clinically a relapse has to last 24 hours and to occur at least 30 days after the previous episode began.

Relapses can vary from mild to severe, and are unpredictable in nature. People with MS fear the residual disability a relapse may cause. In our survey, 78 per cent said that they always or often worry about how their relapse impacts on those around them, 95 per cent were unable to do the activities that they wanted to do during a relapse and 90 per cent felt relapses resulted in a lack of independence. NICE must consider the 'real world' and cumulative impact of relapses on people's day to day lives, and therefore not underestimate the potential for this treatment to significantly enhance quality of life.

2. Avonex is a suitable comparator

The appraisal committee have concluded that Avonex is not an appropriate comparator. The rationale for the committee's decision is based on the following two assumptions: 1. Avonex is not widely used and, 2. Avonex is not as effective as other first-line therapies such as Rebif-44. As a result, the appraisal committee states a preference for the use of Rebif-44 or best supportive care as the main comparators.

In accepting that a DMD in current use in the NHS is not a suitable comparator, we suggest that the committee's reasoning is flawed. All of the 70 MS Specialist centres currently prescribing Rebif-44 also routinely prescribe Avonex. Further, the Department of Health risk sharing scheme (RSS), which has been collecting data for almost ten years and which has published the results of its first two year analysis, has failed to show any difference in efficacy or cost effectiveness between the drugs on the RSS [1] (Boggild et al, 2009).

We do not agree that best supportive care is the most appropriate comparator for the following three reasons:

[1] Boggild, M., Palace, J., Barton, P., Ben-Shlomo, Y., Bregenzer, T., Dobson, C., Gray, R. (2009) "Multiple sclerosis risk sharing scheme: two year results of clinical cohort study with historical comparator", *British Medical Journal* 2009;339:b4677 http://www.bmj.com/content/339/bmj.b4677.full.pdf

i. Best supportive care is not reflective of best practice nor is it reflective of professional guidelines. We are concerned that the impact of a relapse and current UK clinical practice in relation changes a treatment plan have not be adequately considered.

ii. In taking best supportive care as a comparator the relative benefits of a reduced propensity to suffer side effects is negated. Side effects such as flu like symptoms and headaches have a negative impact on people's ability to continue with the activities of daily living.

iii. The Appraisal Committee which reviewed and approved Tysabri (Natalizumab, TA 127) discounted best supportive care as an appropriate comparator. This highlights a significant inconsistency in both NICE's methodology and approach to decision making which needs to be addressed.

3. The proven efficacy of Fingolimod

There is a clear professional consensus that treating people early with the most effective treatment is essential to preserve people's quality of life. Removing the option of an effective treatment would be to condemn some people unnecessarily to a life governed by debilitating relapses and ultimately, progressive disability.

The worrying, painful and distressing nature of a relapse and the loss of independence, are all a fundamental concern for people with MS. The evidence shows that patients experienced a 50-60 per cent reduction in the number of relapses. This is markedly more than the first-line therapies which reduce relapses by 33 per cent. Trial data demonstrates that people taking Fingolimod experienced significantly less deterioration in their ability to carry out daily activities than those treated with beta interferon.

4. Fingolimod addresses an unmet need

Fingolimod addresses an important unmet medical need for the following groups of patients:

i. Those with high disease activity despite treatment with beta-interferon or glatiramer acetate but who do not qualify for Tysabri.

ii. Those who have high disease activity and qualify for Tysabri but do not want to have Tysabri. The risk of developing progressive multifocal leukoencephalopathy (PML) is a factor. It also requires monthly infusions lasting several hours therefore issues related to time (and costs) of infusions and transportation impact on people's decision as to whether Tysabri is a realistic option for them.

iii. Those eligible for Tysabri but who carry the JC virus and are therefore at an elevated risk of PML. The estimates of those who carry the JC virus range

from 20-70 per cent, however a study carried out by Knowles (2006) found prevalence increased with age up to 60 per cent[2]. This group does not currently have an alternative efficacious therapy and face taking a high risk if they opt for Tysabri. Fingolimod presents an opportunity to provide treatment for this group of people with MS.

iv. Those who, although eligible for Tysabri, have had to discontinue because of the adverse side effects. For example, an allergic reaction, or lack of efficacy.

5. The value of innovation

Fingolimod is highly innovative and markedly different from current MS treatment options. As the Kennedy report recommended, innovation should be considered and appropriately weighted as part of the decision making process. Fingolimod meets many of the health-related benefits criteria listed by Kennedy (2009:24)[3] including:

- the ability to offer a different mode of administering a drug - in this case, a tablet rather than an injection or infusion;
- the opportunity to be treated at home rather than attend a hospital or clinic;
- a reduction in unwanted side effects - current DMDs are a significant disruption to the daily lives of over 77 per cent of people affected by MS;
- improvement in quality of life including enjoyment of greater dignity and independence – this treatment will give people with MS and their carers greater freedom;
- the ability to minimise the social visibility of disease or care – a tablet can be taken more discretely and is less disruptive than infusions or injections;
- it has a unique, new mechanism of action (sphingosine-1-phosphate receptor modulator).

It is not clear from the ACD to what extent the above factors have formally been taken into account by the committee, or how each may have been weighted in the decision making process.

Over 95% of 1000 people with MS said that a pill would be their treatment method of choice. NICE must respond to this by giving adequate weight to the scientifically innovative and highly appealing nature of this treatment. NICE should note that the clear preference for a pill as a preferred treatment method is based on the following factors:

- added convenience and therefore enhanced quality of life
- physical and psychological barriers to injecting
- injection site reactions
- ease of administration and less dependence on a friend, family member or carer

[2] Knowles, W.A (2006) "Discovery and Epidemiology of the Human Polyomaviruses BK Virus (BKV) and JC Virus (JCV)",in *Polyomaviruses and Human Diseases: Advances in Experimental Medicine and Biology,* edited by Nasimul Ashan, New York: Springer

[3] Kennedy, I (2009) *Appraising the Value of Innovation and other Benefits A short study for NICE.*

People told us that injecting was taking over their lives where as a tablet could be administered easily and discretely ([4]MSS, 2010:8). The patient expert explained that her experience of the new oral treatment was a very positive one; that it is easy to take, portable and has no side effects (for her). She was able to travel extensively and without it, would not have been able to do her job and continue on her chosen career path. NICE have failed to give adequate weight to the clear preference of people with MS.

Many people with MS find it increasingly uncomfortable to inject and to find new places to inject. People with MS often report experiencing hard and indurated skin. This is supported by our survey where respondents informed us that injections are not a suitable long term method, causing skin reactions, dimpling, stress and anxiety. Therefore to describe injecting as a 'discomfort' in the ACD, fails to capture the real-world physical, emotional and cost impact. It is not just the inconvenience of a treatment but the additional healthcare costs due to extra appointments required to help manage side effects and help with problems related to injecting.

Enhancing quality of life for people with MS and their carers should be a fundamental concern for NICE. We therefore strongly encourage NICE to consider the evidence provided by people with MS regarding their preference for a pill.

6. Wider benefits of treatment

NICE has failed to consider the wider costs and benefits of this drug. As the Kennedy report stated, the wider benefits that should be taken into account include:

- ability to join the workforce
- stay in work or reduce absenteeism
- independence for carers
- reduction in social costs
- increased tax revenue (Kennedy, 2009: 27)

MS symptoms including the emotional and physical impact of MS relapses have a significant effect on people's ability to care for families and or to carry out paid employment. This is of great concern and importance to people with MS as during a relapse, this ability is severely restricted. Research has shown that 37 per cent of people in paid employment had taken over two weeks off during a relapse[5].

This evidence is backed up by the Work Foundation Report[6] which found that only 37 per cent of people with mild MS were working and that many more had to change or quit their jobs due to the fluctuating nature of their MS (Bevan et al, 2011:4).

[4] MS Society (2010) *A submission from the MS Society to inform the NICE appraisal of fingolimod for relapsing-remitting multiple sclerosis*

[5] Data from Zajicek JP, Ingram WM, Vickery J, Creanor S, Wright DE, Hobart JC. Patient-orientated longitudinal study of multiple sclerosis in south west England (The South West Impact of Multiple Sclerosis Project, SWIMS) 1: protocol and baseline characteristics of cohort. BMC Neurol. 2010 Oct 7;10:88. PubMed PMID:20929556; PubMed Central PMCID: PMC2966453

[6] Bevan, S., Zheltoukhova, K., McGee, R. and Blazey L. (2011) *Ready to Work?Meeting the Employment and Career Aspirations of People with Multiple Sclerosis.* London: Work Foundation

Fingolimod offers the potential for many people to continue working and to contribute to society rather than feel frustrated and restricted in what they can do. Current first-line treatments have debilitating side effects and limited impact on reducing relapses, people are therefore forced to reduce their working hours or stop all together. Without taking such evidence into consideration some of the most important factors for a person with MS are being ignored. The report found that on average people with MS are retiring 18 years earlier than the national retirement age. 44 per cent of people with MS retire early in comparison with the 35 per cent European average. 80 per cent of people with MS had retired within 15 years of their diagnosis, severely shortening their working lives[7].

Enabling a person to live more independently, experience less relapses and require less care and support would improve their lives and their carers' lives. The Work Foundation report found that "Professional careers of 57 per cent of relatives are adversely affected by MS of a family member" (2011:4)[8]. The impact on carers should be formally considered in a Technology Appraisal following the recommendation of both the Health Select Committee[9] and the Kennedy Report[10]. The MS Society believes that a wider view should be taken when assessing the cost and benefits of a drug. Societal factors including the ability to work; convenience and innovation such as injections versus tablets; and providing treatment for an unmet need should all be considered.

Fingolimod presents an opportunity to reduce the impact of MS treatment on daily lives; the number of relapses people experience and the care they require. All of these factors will improve the lives of people with MS and their families.

6. Disability and equality issues

Given that there are limited treatments for Rapidly Evolving MS a negative NICE appraisal will exacerbate the inequality in access to treatments. In comparison to other countries in the EU, the UK ranks very low in access to disease modifying drugs (DMDs), only 14 per cent are prescribed DMDs[11].

7. Final comments

It is the profound hope of the MS Society that Fingolimod will be made available to people with MS in the UK. The MS Society urges Novartis to work with NICE and the Department of Health to make this hope a reality, ensuring either a positive final appraisal or the establishment of a patient access scheme.

Contact

If you would like any further information about the points raised in this submission, please contact Daisy Ellis, Policy and Campaigns Officer, MS Society, on 020 8438 0998 or dellis@mssociety.org.uk.

[7] ibid
[8] ibid
[9] House of Commons Health Committee (2002) *National Institute for Health and Clinical Excellence* London: The Stationary Office Limited
[10] Kennedy, I (2009) *Appraising the Value of Innovation and other Benefits A short study for NICE*
[11] Golding, J (2008) *MS Barometer 2008,* European MS Platform. Accessed here: http://www.ms-in-europe.com/w3p_dokumentearchiv/14th_14501515_ms_barometer_john_golding.pdf