Multiple Sclerosis Society

MS Society response to the NICE Appraisal Consultation Document (ACD) on Fingolimod (January 2012)

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 welcomes the opportunity to resolve any outstanding issues regarding this appraisal. However, we remain conscious of the time period it will now take NICE to arrive at a final decision regarding this treatment option. We would like to remind NICE that by the time a final decision has been made this particular treatment will have been licensed for 13 months. We request that NICE do not make this process any more drawn out and lengthy than it needs to be. We sincerely hope that after such extensive consultation, this appraisal will conclude with a positive outcome for people with MS.

We refer NICE to our previous submissions for further detail. Our key remaining concerns are as follows:

1. It is not clear what evidence has been used to support the assumption that one third of people with relapsing and remitting MS who have a sub-optimal response to beta-interferons will receive best supportive care. This seems to be in contrast to the views of clinical specialists.

2. There is no evidence to support the claim that there is a waning of treatment efficacy in Fingolimod yet the cost-effective analysis by the Evidence Review Group (ERG) presents a reduction in efficacy over time. This is in contrast to the two year trial data which showed no reduction in efficacy.

3. The recommendation not to prescribe Fingolimod on the NHS condemns a group of people with no treatment option to progressive disability and higher relapse rates. For those who have not responded to first line treatments, but who are unable to take Tysabri due to risks

of progressive multifocal leukoencephalopathy (PML), there is no alternative treatment.

Relevant evidence and suitable interpretations

Sub-optimal responses

The ACD refers to the ERG's estimation that approximately one-third of people with relapsing and remitting MS have sub-optimal response to beta-interferon treatment and will receive best supportive care. This assumes that they would not try an alternative beta-interferon or choose to try Tysabri. It is not clear what data or evidence has been used to support the claim that one-third receive best supportive care and yet it appears to be central in the rationale for using best supportive care as a comparator. We would like to see evidence upon which this claim is substantiated and call upon the ERG to present their evidence base for this claim.

It is our understanding that this estimation is in contrast with the views of clinical specialists as evidenced by initial research led by Dr Eli Silber and a group of neurologists and MS nurses. Only 4.9 per cent of respondents said that they would stop therapy and offer best supportive care following a relapse whilst on a first line injectable disease modifying treatment.

Optimism versus conservatism

We are greatly concerned that an overly cautious approach has been taken in the production of this second ACD using questionable evidence. The waning of the treatment effect, whilst not proven, is incorporated into the model. The model considers reduction of effect yet there is little explanation of what this is based on. The ERG must provide further explanation of the rationale to explain what evidence there is to suggest that the effects of Fingolimod will reduce over time. We would like to see the evidence used to support this claim such as evidence to suggest if there are any signs that there might be a reduced effect over a longer period of time. Other DMDs have shown that their effects continued for over 10 years. Evidence to show why it is suggested that the effects of Fingolimod would reduce would be welcome.

Following our submission in August we are pleased to see that the Committee has placed a greater emphasis on the innovation that this treatment offers; the reduction in relapses and the reduced side effects. However, we are disappointed that these have not been weighted to their full impact and that the overall impact of having MS is still described as having a 'substantial negative impact on quality of life and activities of daily living'. This condition does not have merely a 'negative impact', it is life altering; MS changes the lives of individuals, couples and families.

This treatment provides a highly innovative method of application with reduced side effects and offers a much higher reduction in relapses than current first line therapies. Whilst the ACD acknowledges this it does not incorporate it into the model. There are numerous examples where we read that a positive impact has not been considered as it was not possible to

establish the exact effect, whereas, possible negative impacts are incorporated into the model. There is concern that this has resulted in an imbalanced pessimistic approach rather than balancing possible negative effects with possible positive impacts.

Equality concerns and discrimination

We are greatly concerned that there is an equality issue that is not being addressed. The place of Fingolimod in the treatment pathway is unique. It provides a new and innovative treatment for a group of people who have previously been left without a treatment option. It fulfils an unmet treatment need.

For people with MS who are not responding to beta-interferons, but due to risk of PML are not able or willing to be treated with Tysabri, Fingolimod offers an important treatment option. There is an unmet need for treatment in this particular group and Fingolimod could provide the first treatment available for people with MS who, to date, have no effective treatment options. Previously this group has been left with one of three options. Firstly, to continue on their current treatment path but with reduced impact; secondly, to be treated with Tysabri despite the risk of PML; or thirdly to give up all treatment options and follow the best supportive care route accepting that this will lead to a possible increase in relapses and ultimately, disability progression. The survey results presented by the neurologists show that for those who fulfil the criteria for Tysabri none would consider stopping therapy; 11.6 per cent would consider escalating to fingolimod; 8.9 per cent would consider changing to another DMT; and 78.6 per cent would chose escalating to a monoclonal antibody therapy.

It is inappropriate to compare Fingolimod with no treatment. People with MS who do not show optimum efficacy on treatments will ordinarily try alternatives and remain on some form of treatment as they would rather be on a treatment, even if it has reduced impact, than no treatment at all. This is a shared view between the MS Society and clinical specialists and is supported by recent survey results which show best supportive care as an option considered by neurologists only once relapse and remitting MS has progressed to secondary progressive MS.

To compare costs of an effective treatment against costs of best supportive care, i.e. no treatment, which puts people on a path of continual disease progression, is highly questionable. To choose to allow a group of people to face increasing disability when they might otherwise be treated and have reduced disability and relapses for some years could be viewed as discriminatory.

Individuals with more active forms of MS should not be excluded from treatment options. Best supportive care is an inappropriate comparator for this new and novel treatment for all the reasons highlighted in previous submissions. As supported by recent evidence from neurologists and MS nurses, best supportive care is a last resort when there are no viable options

and when relapse and remitting MS has progressed to secondary progressive MS.

Best supportive care is an inappropriate comparator for relapse and remitting MS treatments. It does not reflect current UK clinical practice or professional guidelines. Comparing a treatment with no treatment removes the ability to capture reduced relapse rates and relative benefits of a reduced propensity to suffer side effects. The use of best supportive care has previously been discounted as a comparator (TA 127) and therefore we are concerned that there is an inconsistent and unfair approach in appraisals.

Concluding Remarks

We encourage NICE to share the evidence which states that one third of people with relapsing remitting MS who have a sub-optimal response to beta-interferons will receive best supportive care. It is important to understand on what basis best supportive care has been chosen as an appropriate comparator.

We also encourage NICE to share the evidence which supports the suggestion that the efficacy of fingolimod will wane. It is important to understand the assumptions used in the ERG's cost-benefit analysis.

We hope that NICE will include the evidence of the survey results presented by Dr Eli Silber and colleagues in their consideration of fingolimod and consider the place of fingolimod in the treatment pathway.

It is clear that the confusion around the place of fingolimod in the treatment pathway underlines the need to produce a comprehensive prescribing pathway for use in treating people with MS. This also supports the need to fully update the clinical guideline for MS in a truly comprehensive manner which includes all treatments for MS.

We hope that NICE will receive our comments in the constructive manner that they are intended. We urge NICE to continue to work with the Department of Health and the pharmaceutical company to try to find a way forward in order to provide a previously untreated group with an effective treatment option.

Contact

If you would like any further information about the points raised in this submission, please contact [redacted], [redacted], MS Society, on [redacted] or [redacted].