NICE appraisal consultation document for fingolimod

Response from the MS Trust

5th January 2012

Please find below comments from the MS Trust in relation to the second Appraisal Consultation Document (ACD) for fingolimod, published in November 2011. The preliminary recommendation from the Committee in the ACD is that fingolimod is not recommended for the treatment of highly active relapsing-remitting multiple sclerosis (MS).

Our submission will address the following areas, as set out in the ACD, namely:

a. Has all of the relevant evidence been taken into account?
b. Are the summaries of clinical and cost effectiveness reasonable interperetations of the evidence?
c. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?
d. Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

We do not believe that there are any points relating to item D. All our points relate to the first three items for consideration.

1. In our previous submission in response to the first ACD, published in August 2011, the MS Trust made a general observation about the composition of NICE committees. We noted our disappointment that there did not appear to be any member of the committee with specific expertise in neurology. Our view is that this is undesirable and disadvantages the review process, particularly with regard to a complex condition such as MS.

   We also note that the membership of the Expert Review Group (ERG) appears to lack representation from neurology, though there is acknowledgement of the contribution of Helen Ford, MS Neurologist from the Leeds General Infirmary. A number of key issues relating to current clinical practice are central to this ACD and the MS Trust believes that greater involvement from clinicians with specialist neurological expertise in MS throughout the review process would have avoided some of what we believe to be errors in understanding of current management of relapsing-remitting MS.

   We recognise that there were clinical experts present at the Committee meeting in October 2011, but continue to believe that this was insufficient input to ensure that all relevant clinical issues were identified and the clinical context could be adequately described and therefore taken into consideration.

2. The MS Trust maintains that fingolimod is an important additional treatment option for people with highly active relapsing-remitting multiple sclerosis. Disease burden varies between individuals and it is important to recognise that people with MS being considered for treatment with fingolimod have

experienced a significant number of relapses before and despite disease modifying therapy. The case regarding best practice in management of those with highly active disease must be made based on their needs and not on the needs of those elsewhere on the disease spectrum.

3. The Committee has rejected the manufacturer's use of Avonex only as the base-case comparator based on concerns about the implication that a patient may remain on a sub-optimal treatment. They suggest instead that a more appropriate comparator would include alternate first line disease modifying therapy and best supportive care. The Committee has used a comparator composed of equal portions of best supportive care, Rebif-44 and Avonex. The alternative comparator, however, does no better in realistically reflecting clinical practice in the management of relapsing-remitting MS, particularly with respect to the proportion of patients it suggests are receiving best supportive care.

   In section 4.18 of the ACD, it states that

   > *The Committee heard from the ERG that its clinical advisers had estimated that approximately one-third of people with relapsing remitting multiple sclerosis whose disease has a suboptimal response to beta-interferon treatment will receive best supportive care in the UK. The Committee heard from the clinical specialists at the meeting that this estimate was likely to be correct*.

   The MS Trust challenges this assertion. It is important to note that best supportive care means no disease modifying treatment whatsoever. This in no way reflects current clinical practice. Research evidence supports the treatment of people with relapsing-remitting MS early in the disease to prevent axonal damage and irreversible disability. There is evidence that in the target group for whom there is marketing authorisation for fingolimod, progression of disease is likely to be twice as fast as in those with less active disease. Indeed, in section 4.3 of the ACD, the committee heard *'that clinicians are generally reluctant to stop treatment altogether after a suboptimal response.'* Current practice in the management of relapsing-remitting MS is active and acknowledges that even if people with MS continue to have relapses whilst on disease modifying therapy, they may still be deriving clinical benefit from the treatment.

4. The Committee has inconsistently applied its understanding of current clinical practice to its deliberations. The Committee acknowledges that clinicians are generally reluctant to stop treatment altogether after a sub-optimal response to the first disease-modifying therapy used, yet nonetheless applies a comparator which is composed of 1/3 best supportive care.

5. The reality in clinical practice is more complex than is represented in the ACD. Patients with a sub-optimal response to a disease modifying treatment may be offered another first-line therapy or switched to natalizumab. Best supportive care is the least desirable and least common option, reserved largely for when all disease modifying treatments are poorly tolerated or the person with MS has expressed a strong and enduring preference for no treatment.

6. Those patients who don't tolerate the first line treatments face particularly challenging choices. When first line treatments are poorly tolerated by

patients with highly active disease, the current alternatives are severely limited. An oral therapy such as fingolimod would offer a real alternative for patients who otherwise may face the prospect of treatment withdrawal and consequent return of the pre-treatment rate of relapse and risk of axonal damage and increasing disability. Best supportive care in this scenario is neither desirable nor therapeutic.

7. The MS Trust maintains that, in current clinical practice, the proportion of people receiving best supportive care when treatment with a first line therapy is sub-optimal would be significantly lower than other clinical alternatives and this should be reflected in the comparator. Current clinical practice, *as corroborated by a broad cross-section of neurologists specialising in MS* should rightly provide a more plausible assumption about the proportion receiving best supportive care.

8. It is regrettable that there is no opportunity to consider fingolimod in the broad context of the management of relapsing-remitting MS, particularly with respect to natalizumab. The exclusion of those with rapidly evolving severe disease is unfortunate and neglects a group for whom fingolimod may provide a welcome treatment option/alternative. The Committee has been obliged to limit its consideration to the manufacturer's submission.

9. The MS Trust is confident that the Committee understands the serious nature of a diagnosis of MS and the impact of the condition on an individual's ability to remain in work and maintain independence and quality of life. What is less clear is whether a full account has been taken of the negative impact of a relapse on the person with MS or the real cost of a relapse. There are significant health-care related costs of even a single relapse, but additionally there are broader costs in terms of lost income for the person with MS and also potentially for informal carers who need to provide care and support during the disabling period of relapse. No less significantly there are physical and emotional costs to the person with MS.

Conclusion

Research evidence demonstrates the importance of active, early treatment of relapsing remitting MS to prevent axonal damage and avoid irreversible disability. The EMA has licensed fingolimod because it is an effective, safe drug for people with MS who have very few available treatment options. The difficulty in calculating cost effectiveness of MS drugs is well recognised, particularly as the trial data does not address the long-term benefits of treatment.

People with MS in the UK are at risk of lagging even further behind other developed countries in their access to licensed drugs. The MS Trust encourages the Committee to recognise that fingolimod would be an important addition to the small range of available disease modifying therapies for MS and should be made available to those with sub-optimal response to first line therapies. Best supportive care should not be seen as a desirable clinical alternative in highly active relapsing-remitting MS, unless it is the patient's consistently expressed preference.

As with other disease modifying therapies, fingolimod should be prescribed by neurologists, with commencement of therapy and ongoing monitoring provided by specialist MS nurses.