Patient/carer organisation statement template

Thank you for agreeing to give us your views on the technology and the way it should be used in the NHS.

Patients and patient advocates can provide a unique perspective on the technology, which is not typically available from the published literature.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Please do not exceed the 8-page limit.

About you

Your name: [redacted]

Name of your organisation: Multiple Sclerosis Trust (MS Trust)

Are you (tick all that apply):

- a patient with the condition for which NICE is considering this technology?
- a carer of a patient with the condition for which NICE is considering this technology?
- √ an employee of a patient organisation that represents patients with the condition for which NICE is considering the technology? If so, give your position in the organisation where appropriate (e.g. policy officer, trustee, member, etc)

  [redacted]

- other? (please specify)

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

1. **Advantages**

(a) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make.

MS remains a difficult condition for both the individual given a diagnosis and the health service. The fact that we still do not know the cause and to date we have no cure means that for people given a diagnosis and their families they face a very uncertain future for the rest of their lives. MS only reduces life expectancy by a minimal amount probably no more than seven years, so an individual may have MS for 30 – 40 years.

People with MS are usually diagnosed in their mid 20s or 30s and this is a time when many life decisions are made. These become very difficult with the uncertainty of MS and for many people the thought of life with significant disability can be a major barrier to progress. MS remains the greatest cause of disability in young adults.

MS therapy is based on three main aims namely treatment of acute relapses to relieve relapse related symptoms, disease modifying therapy to achieve a long-term delay in the course of the disease and symptomatic therapy. NICE has stated in the scope for this STA that “Corticoid steroids are also sometimes used for managing relapses”. We would challenge this statement in that corticosteroids can provide relief from the symptoms of a relapse but they cannot manage the incidence of relapses.

To date we do not have any drugs which can cure MS and thus the hope of more effective agents remains. The availability of Fingolimod would therefore provide a new disease modifying drug to add to the current range which would enhance the chance of therapeutic efficacy. As in other areas drug development is sequential and it would seem that Fingolimod is more efficacious than some of the current drugs and has an improved method of administration, although the potential side effects are greater than the original disease modifying drugs, interferon beta and glatiramer acetate. The side effects however seem to be less severe than in some of the other new drugs being developed for MS.

Fingolimomd is a new class of agent – a sphingosine 1 phosphate receptor modulator. Fingolimod can be classed as an immunomodulatory drug and it acts by preventing the lymphocytes from leaving the lymph nodes so stopping them from mounting immune attacks including the autoimmune attack in multiple sclerosis.

There are two large trials for Fingolimomd which have been published and presented at major symposia. The FREEDOMS study is a placebo based study using two doses namely 0.5mg and 1.25mg and involving 1,272 people with relapsing remitting MS. It is our understanding that the 0.5mg dose is the one which is being reviewed by the EMA for licensing. The other study is the TRANSFORMS study using the same two doses of Fingolimod against interferon beta 1a in 1,292 people with relapsing remitting MS. Patients in both studies have been given the chance to continue in an extension study. The level of data and years of usage of Fingolimod is therefore significant, although as with all drugs for a condition like MS the level of usage in a clinical trial is inherently shorter than usage in real life, so side effect monitoring will be needed in clinical practice. There is some evidence that Fingolimod may have an effect on nerve repair “neuroprotective” but this is being investigated further.

(b) Please list any short-term and/or long-term benefits that patients expect to gain from using the technology. These might include the effect of the technology on:

- the course and/or outcome of the condition
- physical symptoms
- pain
- level of disability
- mental health
- quality of life (lifestyle, work, social functioning etc.)
- other quality of life issues not listed above
- other people (for example family, friends, employers)
- other issues not listed above.

Fingolimod has the following benefits for people with MS:

1. Relapse reduction

Research undertaken by the MS Trust showed that relapses have a significant adverse effect on quality of life for people with MS. A relapse lasts on average 55 days and with individuals having two or three relapses per year a significant percentage of the year may be blighted by the individual feeling very unwell, being unable to work, or enter into leisure or family activities.

The Fingolimod FREEDOMS study showed a relative reduction of annualised relapse rate of 54% for the 0.5mg dose. This dose is the one we understand being considered by the regulatory authorities. The results were against placebo during a 24 month study. Analysis of subgroups within the study showed that the annualised relapse reduction took place irrespective of patient gender, disease severity assessed by baseline EDSS or gadolinium enhanced lesion load, or treatment history.
The relapse rate remained low in the study for a period of over 100 days after discontinuing Fingolimod, while MRI activity returned to baseline values within 90 days without any evidence of rebound above baseline values.

In the other Fingoliomd study TRANSFORMS the relative reduction in relapse rate was a reduction of annualised relapse rate of 52% versus interferon beta 1a. The actual figures were 0.16 relapses at year one for the 0.5 mg Fingolimod compared to 0.33 for beta interferon 1a.

Of special interest is the Fingolimod data which showed a significantly lowered rate of relapse requiring steroid use or hospitalisation compared with interferon beta 1a in the TRANSFORMS study.

As stated above relapses have a significant impact on how well a person with MS can live their life and thus a reduced amount of time in hospital or on steroids will bring immediate benefits.

2. Reduction in disease progression and thus reduced disability

In the FREEDOMS study the reduction of disability was 30% in the 0.5mg dose as compared to placebo. The cumulative probability of disability progression (confirmed after 3 months) was 17.7% with 0.5mg Fingolimod , 16.6% with 1.25mg of Fingolimod and 24.1% with placebo.

Both Fingolimod doses were superior to placebo with regard to MRI related measures (number of new or enlarged lesions on T_2 weighted images, gadolinium enhancing lesions, and brain volume loss for all comparisons at 24 months).

With trials of the length undertaken to date evidence of lack of disease progression is less certain, but the relapse reduction evidence is prognostic for disease progression benefit.

3. Quality of life benefits

In the TRANSFORMS study the PRIMUS – Activities scale was used to assess changes in daily functioning of patients. This is a patient reported outcome measure for activity limitation. The PRIMUS scores were recorded at baseline, six and twelve months. After 12 months patients treated with oral Fingolimod at either the 0.5mg or 1.25 mg dose experienced significantly less deterioration of their ability to perform daily activities compared with patients on interferon beta 1a.

4. **Other benefits**

People with MS have a significantly higher rate of depression than the normal population with in excess of 50% of people with MS having an episode of clinical depression during the course of their disease. Active management with an agent such as Fingolimod which is easy to administer is likely to help people with MS feel in control of their condition and thus reduce the level of depression.

Other issues related to MS such as fatigue, pain and cognitive dysfunction may be reduced by the administration of Fingolimod although there does not appear to be conclusive evidence as yet.

The fact that Fingolimod is an oral tablet does have advantages over the current injectable or infusion agents. It will be easier to administer, and one would anticipate that compliance will be higher.

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

2. **Disadvantages**

Please list any problems with or concerns you have about the technology. Disadvantages might include:

- aspects of the condition that the technology cannot help with or might make worse.
- difficulties in taking or using the technology
- side effects (please describe which side effects patients might be willing to accept or tolerate and which would be difficult to accept or tolerate)
- impact on others (for example family, friends, employers)
- financial impact on the patient and/or their family (for example cost of travel needed to access the technology, or the cost of paying a carer).

1. Side effect profile

Macula oedema and hypertension were more common in the Fingolimod group than in the control group in the clinical trials. The 0.5mg dose was generally better tolerated than the 1.25mg and as it is the lower dose that is going through licensing the side effect profile will be better. However, it is clear that people on Fingolimod will have to be monitored for adverse events.

An asymptomatic elevation of liver enzymes was also seen in approximately 10% of patients in the trials with the levels being 3 –fold in comparison to the placebo group. As stated above monitoring will have to be undertaken for people on therapy.

There is also an increased risk of viral infections with the drug. Considering the mode of action of Fingolimod one might fear a possible rise in cancers with usage. Whilst this does not seem to have been seen in the phase lll trials we hope that close surveillance would take place in clinical practice.

2. Usage in women

More people with MS are female (3:1) and thus of child bearing age. To date we are not aware of the situation with regard to pregnancy and usage of Fingolimod.

3. Level of monitoring

We understand that people will be specifically screened prior to starting Fingolimod and also when they take their first dose. Ongoing monitoring will also be required, and it is at present unclear as to how onerous the monitoring will be for patients, although previous experience would suggest that people with MS respond well to ongoing monitoring.

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

An oral presentation is a very attractive option for people with MS.
There has been a significant level of awareness of the oral drugs in development and some mis-understanding amongst people with MS about the differences between the new oral agents such as Fingolimod and those currently available. We know that everybody finds the assessment of efficacy and risk difficult and people with MS are no exception. For the person with MS their attitude to risk will be different from the general population and also different depending on the activity of their disease.
For MS therapies to be maximally effective they should be started early prior to neuronal damage and this makes risk assessment harder. We anticipate a change in the neurology teams to enable a greater discussion to take place with patients to ensure that the efficacy and risk are fully explained prior to initiation of therapy.

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?

We are submitting this response in advance of the licensing decision and also without in depth knowledge of any subgroup analysis that may have taken place on the clinical data.

We hope that Fingolimod will be licensed for relapsing remitting MS.
In the first instance we suspect that clinicians would use Fingolimod in relapsing remitting MS patients who have failed on current therapies, in patients where the slightly higher risk is justified by the level of their disease activity and where an injection routine is out of the question. With enhanced UK clinical experience we would anticipate a broadening of usage but we do not see Fingolimod replacing the current drugs, rather being an additional agent.

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.

The current drug therapies that are available are:
Avonex – interferon beta 1a
Betaferon and Extavia – interferon beta 1b
Rebif – interferon beta 1a
Copaxone – glatiramer acetate
Tysabri – natalizumab

They are all indicated for relapsing remitting MS although Tysabri has an indication for highly active relapsing remitting MS in order to balance its efficacy with its side effect profile. The beta interferons and glatiramer actetate are equally effective in terms of reduction of relapses but the data on long-term disability varies between the products.

Clinical usage of the beta interferons and glatiramer acetate over a period of fifteen years in the UK, and longer in the USA, has shown that they are very safe.

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

- improvement in the condition overall
- improvement in certain aspects of the condition
- ease of use (for example tablets rather than injection)
- where the technology has to be used (for example at home rather than in hospital)
- side effects (please describe nature and number of problems, frequency, duration, severity etc.)

Fingolimod appears to reduce relapse to a greater extent than the original disease modifying drugs namely the beta interferons and glatiramer acetate, although only one direct study has been undertaken against interferon beta 1a. It has not been directly compared with Tysabri which in the UK holds a licence for highly active relapsing remitting MS alone.

Fingolimod as an oral preparation would have a significant advantage from a patient perspective when considering convenience, and thus possibly adherence.

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

- worsening of the condition overall
- worsening of specific aspects of the condition
- difficulty in use (for example injection rather than tablets)
- where the technology has to be used (for example in hospital rather than at home)
- side effects (for example nature or number of problems, how often, for how long, how severe).

It is still unclear exactly what pre-assessment routine will be followed or what ongoing monitoring will be required. It is therefore impossible to discuss any possible disadvantages. However, it would be positive to have another disease modifying drug available to add to the treatment options, allowing the most appropriate product to be used in each circumstance.

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.

We have not had any direct contact with people who have been on the Fingolimod trials and cannot thus make any comment on their views.
As stated above we do know that people with MS would welcome an oral form of administration.

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

Not applicable

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 MS Trust is aware of a web-based survey undertaken in April 2010. We have spoken to people with MS who have completed this survey and who are angry and concerned by its content.
The problem with any such survey is that if you ask anybody whether they would like an oral tablet versus an injection the answer is clear and everybody would prefer an oral tablet. The survey did not allow participants to state how they would rank oral administration alongside safety, and thus risk, over the current drug therapies.

In essence the MS Trust believes that efficacy and safety are paramount and at present it is difficult for people with MS to have an accurate perception of Fingolimod or any other oral drug in development.

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?

Multiple Sclerosis remains a cause of severe disability for many young adults and for anyone given a diagnosis of MS their life will never be the same again. The current drugs have demonstrated some efficacy but greater efficacy would undoubtedly be beneficial and thus Fingolimod should be available on the NHS but prescribed within the environment of a specialist MS service.

Reduced relapses and less disability would have a major impact on the quality of life of the person with MS and also on their families and friends.

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

MS in the UK has for many years felt the second class citizen when compared to all other parts of the world. In the USA circa 60% of people with MS are on the current drug therapies, the figure for Europe is 30% but in the UK only approximately 14% of people are currently prescribed drugs. If Fingolimod is given a licence by the regulatory authorities but is not made available on the NHS it will further entrench the view amongst people with MS that their lives are not valued in the UK.

All the research evidence shows that it is desirable to treat people with MS early in their disease course prior to axonal damage and delays cannot be reversed. Any delays to treating an individual, or not allowing routine usage within the NHS, will mean that the individual will have to live their life with accrued disability.

Whilst it is difficult to demonstrate cost efficacy within MS, it must be considered that people with MS can be a huge drain on UK plc if they are no longer able to work. Currently 60% of people with MS are out of work within five years of diagnosis. All the drug therapies have the potential to improve this statistic and should be available on the NHS. In addition the cost of

caring for people with MS in the UK is very significant and whilst this is often done by a family member it cannot be discounted in the assessment.

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

No

Other Issues

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