NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Dimethyl fumarate for treating relapsing-remitting multiple sclerosis

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:
Patient Representative nominated by the 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)
- other? (please specify)

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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.

Greater efficacy at reducing relapse rates compared to current disease modifying drugs

The significant reduction in relapses (up to 53% in phase III clinical trials DEFINE and CONFIRM, compared to placebo, up to 23% more than current first-line DMDs) would meaningfully diminish the interruption of disease activity to the lives of people living with MS. The reduction of relapses would significantly decrease the arrival of new physical symptoms (eg. muscle weakness, impaired bladder and bowel function, spasticity, ataxia, optic neuritis) and reduce the accrual of residual disability (see below), reduce hospital admissions, increase employability for MSers, increase quality of life dramatically, improve mental health (due to less life disruption), ensure continued social interaction.

Consequent Avoidance of Residual Disability

I, like many people with MS, incur substantial residual disability with every relapse. Most significantly with every relapse my gait and mobility deteriorate sharply. This impacts on my ability to travel for work, my fatigue levels and my employability in general. It also impacts on my quality of life, impedes my general (ie cardio vascular fitness) and my prospects for reasonably healthy, independent longevity. Since relapses have limited my ability to exercise energetically or for a long period of time, the chances of my having complications due to MS are increased.

The provision of dimethyl fumarate (DF) would limit the chances of further accrual of disability and complex disabilities hence improving MSers chances of long term survival through avoidance of life threatening complications due to MS. The provision of DF would be a cost effective step for the NHS/State, significantly increasing the chances of keeping myself and others with MS in employment, paying tax, and imperatively less dependent on NHS and social services.

Practical /Convenient Route of Administration

The simplicity of administration of dimethyl fumarate would be cost effective for the NHS who currently have a range of instruction, monitoring and infusion tasks around the supply of DMDs for MS.

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Patient compatibility/safety
The administration of dimethyl fumarate results in minimal side effects, unlike other first line therapies for MS whose side effects range from injection site reactions to death or severe brain damage. For those who are incompatible for other treatments (ie JC Virus positive for Natalizumab) it provides an efficacious alternative.

(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.

The course and/or outcome of the condition
Physical Symptoms
In DEFINE phase III clinical trial dimethyl fumarate over a two-year period the risk of sustained disability progression was reduced by 38% compared to placebo. Indicating a significant improvement in the course of the disease.

The Relapse rate has in Phase III trials been reduced by up to 53%, reducing the need for hospital admissions or IV steroids by 48%. Reducing costs for the patient and the NHS.

I am now intolerant of corticosteroids and hence am not able to get **the anti-inflammatory benefits** of steroids, which provided significant enhancement of my physical abilities. Dimethyl fumarate would provide a safe, long term anti-inflammatory treatment. This would provide a significant improvement in my day to day functioning.

Likewise the neuroprotective elements would provide improved protection against demyelinating attacks on the brain and spinal cord.

Level of Disability

As outlined above DF would have an impact on disability progression in the short term.

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Mental Health
Quality of Life

As indicated above and in my experience, fewer interruptions to work, social life and improved quality of life aid improved mental health for people with MS. Over 50% of people with MS experience an episode of depression during the course of their disease.

Combining data from DEFINE and CONFIRM, DF resulted in significant improvements in physical and mental aspects of health and functioning compared to patients on placebo.

From my own experience I can confirm that increased incidents of relapse and disease progression provoke an unsettling impact on mental health. Dealing with the unpredictability of MS is extremely challenging for even the most resourceful and resilient people.

Increasing stability in MSers' conditions (ie through DF) would provide a greater sense of well-being, promote mental health and provide greater opportunity for exercise and general wellbeing. DF has the ability to do this.

Other People
MS is characterised through a dependence on others in the short term during relapses and looking to the future, through the need for considerable informal and formal care. DF's ability to reduce relapses and slow disability progression, would improve *independence of MSers* and further reduce the economic impacts of MS in the short term by the interruptions brought about through relapses and the long term for slowing the need for informal care from family and partners.

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).

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As indicated above side effects of DF are comparably mild, when contrasted with other MS treatments but may result in a lower adherence to the drug taking regime, or stopping.

I can not see any other disadvantages to the drug.

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

In my experience of talking with other relapsing remitting MS patients, there is an excitement about DF and no differences to this 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?

People who are JC Virus positive and hence may come off Natalizumab, would benefit from having a neuroprotective treatment to move on to that is also efficacious.

Those moving away from other first-line self-injectable DMDs, due to skin issues and failing on the treatment could benefit considerably.

Comparing the technology with alternative available treatments or technologies

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

(i) Please list any current standard practice (alternatives if any) used in the UK.
Avonex - interferon beta 1a
Betaferon and Extavia - interferon beta 1b

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Rebif - interferon beta 1a
Copaxone - glatiramer acetate
Tysabri - natalizumab
Gilenya - fingolimod. Approved by NICE as a second line treatment when relapse rates remain unchanged or increase despite at least 12 months beta interferon treatment.

(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.)

Beta interferons and glatiramer acetate reduce relapse rates by approximately 30%, dimethyl fumarate by approximately 50%. The significant improvement in efficacy with DF, as well as a simpler method of administration make it obviously advantageous.

Natalizumab is approved by NICE for people with rapidly evolving severe MS; it appears to have a greater efficacy than dimethyl fumarate although the two drugs have not been compared in head-to-head clinical trials. Yet if like myself you are found to be JC Virus Positive, the treatment comes with a risk of mortality or severe disability, that inhibits mental health and causes understandable concern in the MS community. In addition like myself, your disease may be rapidly evolving (relapses and significant progression of disability) but you can still find yourself ineligible for this treatment and having to remain on ineffective beta interferons or gamma acetate.

(as per MS Trust)
Fingolimod is approved by NICE as a second line treatment only after 12 months of beta interferon treatment. This has created a roadblock in the treatment pathway for people who continue to relapse with glatiramer acetate, as they will only be eligible for fingolimod if they switch to one of the beta interferons for a further 12 months, which are unlikely to be more efficacious. For patients the most important issue is getting access to the right drug at the right time and not experiencing needless, avoidable and burdensome delay. The same problem will arise for those who continue to relapse while taking dimethyl fumarate or one of the other new disease modifying treatments currently going through licensing and appraisal. While we recognise that this situation results from the wording of the EMA licence for fingolimod, we wish to flag up the clinical issues it has created and urge NICE to consider how this could be resolved in the best interest of patients and the NHS.

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(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).

(as per MS Trust)
None, although as noted above it is unclear how people will tolerate side effects of dimethyl fumarate (GI events and flushing) in routine use.

Equality and Diversity

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- Could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- Could lead to recommendations that have any adverse impact on people with a particular disability or disabilities

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts

None

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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.

(See MS Trust response)

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

None that I'm aware of.

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.

No.

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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?

- Reduction in debilitating MS relapses for people with RRMS
- Reduction in the accrual of residual disability for people with RRMS
- Less reliance by people with MS on NHS services in the short term. Fewer hospital admissions, visits to A&E or GP, less physiotherapy sessions (rehab from relapse), fewer psychology appointments, less dependence on corticosteroids for relapse treatment.
- The slowing of disability progression would mean a higher quality of life for those with MS in the short to long term, with greater employability options, increased sociability and engagement in society.
- Enhanced adherence to a DMD regime through DF's ease of administration
- Reduced care burden for informal and formal care for MS

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

Not making the technology available on the NHS would be a costly move in terms of the long term care and treatment of the growing community of people with MS. It would inhibit patients ability to contribute to the economy and society, on a par with others.

Seeing as this technology has been licenced for use in Europe, it would be unfair for this treatment not to be available in the UK for patients, especially in considering DF's efficacy and safety

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

No.

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