## 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: Nicola Russell**

**Name of your organisation: Multiple Sclerosis 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?

**X** 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) **Director of Services**

- 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.

Multiple Sclerosis (MS) remains a condition which is not fully understood despite it being first described in 1868. There remains no cure and people are classically diagnosed in their mid twenties to mid thirties.
MS is therefore a condition where people live most of their adult life with their MS and MS remains the greatest cause of disability amongst young adults.
The lack of any medicines which are fully effective means that all new drugs offer a new hope for improved efficacy and thus a reduction of disability for people with MS.

To date there has been limited published data on oral Cladribine with just one study in relapsing remitting MS, published in the New England Journal of Medicine, Jan 20th 2010, though there have been previous studies of intravenous or subcutaneous Cladribine in MS. Two other phase three trials of oral Cladribine are close to completion ("ONWARD" and ORACLE MS").
From the NEJM study it is clear that Cladribine will:

1. Reduce the number of relapses that an individual will have. Relapses are a huge problem for people with MS especially if they are trying to hold down a job, run a family etc. Research undertaken by the MS Trust showed that on average a relapse lasts 55 days a not insignificant period, especially if an individual is having two or more relapses a year. In the scenario of two relapses 30% of the year could be lost with the individual unable to participate in normal activities. A drug that reduces relapses is therefore very important and Cladribine in the published study had a greater effect on relapses than the currently available licensed drugs (though it was not directly compared with them in the trial).

2. Reduce disease progression. During the 96 week published study there was a relative reduction in the risk of 3-month sustained progression of disability in the Cladribine treated groups. However, this is a short trial duration treating relapsing remitting patients which makes the assessment of progression problematic.

3. Reduce lesions in the brain as demonstrated by MRI. MRI has become the mainstay of MS diagnosis and investigation over the last twenty years, and in the published study Cladribine reduced the number of lesions as shown on serial MRI. Reduced MRI lesions, although not directly linked to clinical manifestations, indicates reduced disease activity.

(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.

One of the ongoing problems with MS as a condition is that it is endlessly variable. It is both variable between different people with MS but also for an individual the condition can vary from day to day and hour to hour. This makes it a complex condition to study and also an exceptionally difficult condition to live with; planning for the future becomes a complete lottery.

Patients treated with Cladribine can hope for an improved quality of life due to reduced relapses. As a relapse can vary from optic effects through to loss of bladder control, or even paralysis any reduction in the number of such episodes significantly reduces the mental and physical burden of MS.

Depression is significantly higher in the MS population with in excess of 50% of people with MS having clinical depression at some stage. By helping reduce the number of relapses Cladribine is likely to reduce the level of depression.

Other symptoms of MS such as fatigue, pain and cognitive dysfunction may be improved with Cladribine but we have not seen any such data yet.

The positive effects of Cladribine will help not only the person with MS but also their friends, family and employer by enabling the individual to live a more normal life.

**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. At present it is difficult, due to lack of published data, to understand the possible adverse effects of Cladribine. It is clear that Cladribine has a significant impact on the immune system targeting immune cells implicated in the pathogenesis of MS. The trials of Cladribine have involved a short course yearly dosing regime and this indicates a long half-life of the active ingredient. This long half-life might be problematic if restoration of full immunocompetence is needed quickly.

2. MS affects primarily women and most commonly they are of child bearing age. It will be important to know if there are any adverse effects in the long-term and so far we do not have this data.

3. When side effects did occur in the trial they were serious including lymphocytopenia, and herpes zoster infections. Neoplasms were also reported in some patients.

4. The current trial has been done in relapsing remitting MS in a relatively small number of patients, over a relatively short period of time. Further side effects may occur when the product is used over a longer period of time.

For all the reasons stated above the pre-assessment and post prescription monitoring of patients on Cladribine will be critical and will need to be undertaken by appropriate neurologists.

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

The currently available drugs for MS are either self injection therapies or an infusion given within the hospital environment. The concept of an oral therapy is therefore very attractive.

There has already been a level of public awareness promoting the oral concept and currently there is an interesting divide between people with MS who are convinced that oral therapies will provide the solution and those that are doing well on the current therapies.

When Tysabri was in its clinical development stage it was also hailed as an agent offering greater efficacy than the then currently available drug therapies. With greater usage the possibility of the serious side effect of PML was identified and there have now been in excess of 40 cases of the potentially fatal PML identified world wide. Tysabri remains a very effective agent and also exemplifies the increasing complexity of MS management where the more powerful the drug the greater the risk.

For people with MS risk is different from risk for a healthy individual. However, it is clear that to expect a person with MS to fully understand their level of risk, when their disease might still be mild in the early relapsing remitting stage, is difficult. It is also clear that it will be imperative that the potential benefit of ease of administration with Cladribine does not cloud the assessment of risk.

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?

As we are submitting this response prior to a licence being granted for Cladribine, and with only one published clinical trial this is a difficult question to answer.

The clinical trial of Cladribine to date has been done in relapsing remitting MS and this is set alongside the recent research evidence which shows that it is best to treat MS early prior to axonal damage. We would therefore anticipate that in the first instance Cladribine should be used for the treatment of active relapsing remitting MS.

**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.)

Cladribine offers a greater reduction in relapse rate than the beta interferons and glatiramer acetate although there have been no direct comparative studies.

An oral tablet would be a significant advantage for patients although many people settle well into an injection routine, in the same way as insulin dependent diabetics. It is also true that for most people the injection element of drug administration reduces once they have done their first injection, and the actual fear of injecting is overcome.

(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 unclear at present exactly what pre assessment procedures will have to be followed for Cladribine, what assessment will be needed during the administration phase, or what post prescription. Until this is clearer it is impossible to be dogmatic about any potential disadvantages or benefits.

As mentioned earlier the fact that Cladribine has a long half life may be problematic for some patients if they need to return to full immunocompetence quickly. It is not known yet what effects there might be in pregnancy.

**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.

Cladribine has yet to receive its licence and has thus only been used to a very limited extent within the UK at the six centres who participated in the clinical study. There has been no routine clinical usage and thus the MS Trust has had very little contact with any people taking Cladribine.

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

N/A

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 during April. 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 this feature of Cladribine 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 Cladribine.

**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 Cladribine 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 Cladribine 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.

**Other Issues**

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