# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

## Alemtuzumab for the treatment of 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:**

**I am a patient who has received treatment with alemtuzumab for relapsing-remitting multiple sclerosis. I have also been interviewed by a representative from the MS Society, and the content of that interview comprises part of the statement submitted by the MS Society for this appraisal. I agree with the content of the MS Society statement but also now submit this additional statement as an individual patient expert.**

**Are you (tick all that apply):**

- a patient with the condition for which NICE is considering this technology? **YES**
- a carer of a patient with the condition for which NICE is considering this technology? **NO**
- 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). **NO**
- other? (please specify) **N/A**

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

**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.

Physical and mental well-being
Speaking personally, since my last treatment with Alemtuzumab in 2007 I have had a year-on-year improvement in both my physical and mental health, suffering from far fewer relapses (less than 1 a year) and with no accumulation of disability. In fact, my health has continued to improve to a level that I experienced before my diagnosis, allowing me to work full-time, volunteer extensively, care for family and have an active social life. The 'relapses' I do experience are always linked to times where I have slept badly for days on end, when the daily temperature is high for long periods or when I am seriously overdoing things; in fact both my partner and I welcome the re-visitations of old symptoms – normally a tingle in my right hand, low mood and an appreciable slowing of my ability to parallel process complex tasks – as a warning to slow down and rest. Once I have done so, the symptoms vanish leaving no disability.

Reduction in severity and frequency of relapses
MS is an unpredictable chronic condition, where relapses can occur at any moment without warning and can affect life to a considerable degree (for example, walking, vision, painful muscle spasms etc). This treatment greatly reduces the number of relapses an MSer experiences, and when relapses do occur they are generally much less severe and last for a shorter period. This alone is a hugely positive outcome of treatment. In the year before my diagnosis and the six months following it I experienced a range and frequency of new symptoms that brought life to an absolute stop for me and my partner, causing us both extreme stress, anxiety and depression and making us scared for what the future might hold. Since my second treatment in 2007 I have experienced only a handful of new symptoms in eight years and the occasional 'reminder' symptom when I overdo things; these are more like 'friendly warnings' to slow down and rest than scary potential disabilities – and I have had no accumulation of disability from any symptom since my treatment.

Decreased long-term accumulation of disability
Although the unpredictability of the condition in terms of when the next relapse will occur and what aspect of life it will affect be is bad enough, I knew that even an apparently benign condition would inevitably progress over my life towards an accumulation of physical and mental disability that was devastating in the short-term and worrying in the long-term. The fact that treatment with Alemtuzumab greatly reduces the rate of sporadic relapses and the accumulation of disability with each relapse, as well as effectively 'freezing' the condition at the level of accumulated

disability is hugely important. In my case, the level of accumulated physical and mental disability has actually been reduced in the long-term following treatment.

Allowing patients to lead a normal life; long-term improvement in quality of life
A diagnosis of multiple sclerosis means that a patient is always aware of their condition and it comes to rule their life – one is always weighing up what activities might result in stress or tiredness and potentially lead to a relapse. This affects social activity, what work one might choose to do, whether one can fulfil caring duties for others, how active one's life is, even whether to have children. As many MSers find themselves unable to cope with full-time employment within a few years of diagnosis, their quality of life often deteriorates, leading to depression and anxiety on top of their MS. After treatment with Alemtuzumab the course of one's MS is much more predictable both in terms of relapses and disease progression, and I certainly felt as though I had been effectively put back into control of my life. This is a huge improvement, allowing MSers to be 'normal', to work and make a contribution to society that in turn greatly increases the quality of life for both the patient, friends and family and their community.

Decreased reliance on family, friends, carers and social care/benefits

The majority of patients diagnosed with MS will inevitably experience increasing levels of both physical and mental disability - even if they are able to access current treatments. Within a few years of diagnosis many will be working only part-time and even between relapses will experience anxiety, depression, a reduction in social activity and a greater reliance on friends, family and caring services to get them through the day. Many will eventually cease to work at all and rely on social care and benefits. The reduction in rate of relapses, the reduction in the rate of accumulating disability and the increased quality of life and independence given by treatment with Alemtuzumab and described above mean that the patient remains a useful and productive member of society for longer – and the unstated burden of care that often falls onto family and friends (impacting greatly in turn on their quality of life) is also greatly reduced. It also means that the implied future impact on social care services and the welfare state for each person diagnosed with MS is less.

(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.

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

'One-off' administration of treatment
Currently other MS treatments require patients to take a daily pill or to self-inject on a regular schedule, requiring medication to be securely delivered to their home and stored correctly even before they overcome the natural squeamishness of injecting and deal with adverse site reactions and side-effects. It is a constant reminder of their condition, and often restricts social activity (for example when and where they are able to holiday). Even before the possibility of treatment with alemtuzumab, I had decided that the treatment sounded worse than just living with MS (even though the thought of that was terrifying) and so refused to even contemplate any self-administered injectable DMD. In contrast to this, Alemtuzumab is administered by trained staff in hospital over the course of a few days when needed and in between the patient doesn't have to deal with any medication or issues arising – greatly increasing adherence to medication, and providing the safety-net of trained staff on hand if there are any treatment issues. Personally speaking, I found it a great relief to leave the hospital after treatment and – except for follow-up visits and blood tests – to begin to lead a 'normal' life where I could forget about my MS, go back to full-time work and enjoy a social life. Within two months I was able to fly to the States for work, and when the second treatment came round it was a shock to realise a year had past.

Effect on family & friends
The impact of my diagnosis on my partner, family and friends was devastating, and the stress led to physical and mental health issues for my partner, as well as requiring him to take extensive time off work both at the time of diagnosis and during my first treatment with Alemtuzumab. Since then there have been no further issues, and he is able to work full-time as I need no further care. He tells me that he no longer as to watch me daily to check on my health.

**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).

In-patient administration of medication
Although listed above as an advantage, the fact that Alemtuzumab is only able to be administered to an MSer as an inpatient might be seen as a disadvantage, requiring

time off work, travel to hospital and a stay in hospital. This will also impact on the family of the patient.

Short-term side effects
The short-term side-effects of Alemtuzumab are immediate but well-understood and usually effectively dealt with during the transfusion. They include (and I experienced) headaches, fever, chills, extreme fatigue and a temporary return of old symptoms. I also experienced a spectacular (but non-itchy) rash over my entire torso that faded over two days. However, the majority of these side-effects are short-lived and disappeared within a few weeks of treatment.

Impact of on-going monitoring
The necessity of monitoring the re-development of the immune system following treatment means that blood tests must be taken on a regular schedule for at least three and possibly five years following treatment (starting at once a month and reducing to annual over time). This can become an issue!

Possible development of other auto-immune conditions
The most serious potential side-effect of treatment is the development of other auto-immune conditions as the immune system re-establishes itself. However this risk is considerably lower than initially thought, understood and stressed to patients and their GP and can be easily monitored using blood tests, and patients given immediate care and treatment for any issues.

Possible anti-Alemtuzumab antibody development
Due to the way that Alemtuzumab works – by destroying certain types of immune cells – and the fact that it is itself a protein-based antibody, it is possible for the patient to develop antibodies themselves against Alemtuzumab. This potentially restricts the number of times Alemtuzumab can be usefully administered over the life course.

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

As far as I know, there are no disagreements about the effectiveness of this treatment – just concerns about the fact that it is not universally available except to the very lucky through clinical trials (now ceased).

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?

Those patients who have been diagnosed with relapsing-remitting multiple sclerosis, especially with an active or aggressive condition, will benefit hugely from this treatment. Unfortunately people with secondary progressive or primary progressive

forms of the disease may not benefit from the treatment, although as far as I know they have not formed part of the clinical trial cohort.

**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.

Currently it appears to be a bit of a lottery as to whether a newly diagnosed person is offered disease-modifying treatment or not. Those currently on offer include a range of injectable drugs (with all of the associated down-sides) that require administration once every few days – constantly reminding the person of their condition and restricting their life considerably. A step forward came recently with the development of an oral pill to be taken once a day, removing the requirement for self-injecting. These DMDs include: Tsybari, Beta-feron, Gilenya, Avonex, and Rebif

(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.)

<u>'One-stop' administration of medication</u>
Although Alemtuzumab has to be administered to patients in hospital by infusion over several days, the fact that it only needs to be done once a year for two years (and then again only as necessary) makes it far less of an issue than a regular self-injection or a daily pill. As the majority of the side-effects arise during the transfusion period, this means that patients are sure of immediate care and treatment for these and support and monitoring of their condition in the long-term. The 'one-off' nature of treatment also means that sticking to a treatment schedule is far easier, far less disruptive to a normal life and is not the daily reminder of illness that current treatments are.

<u>Clear long-term benefits</u>
Alemtuzumab offer very clear long-term benefits to those treated – not just a huge reduction in the frequency of relapses, but a reduction in the severity of those relapses and the disability that inevitably accumulates over the lifelong course of the disease. While other DMDs offer a reduction in the rate of relapses, it is a far smaller

reduction than Alemtuzumab offers, and other DMDs do not also offer the reduction in accumulated disability that Alemtuzumab does.

(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).

In-patient administration of treatment
As stated above, the necessity for Alemtuzumab (currently) to be administered by qualified medical staff as an inpatient stay is different to current treatments that are administered at home by patients themselves. This may be seen as a disadvantage by some patients, and may cause some disruption to their work, family life etc.

Short-term side-effects
The immediate side-effects of treatment are stated above, but are well-documented and easily dealt with in the first instance while the patient is still in hospital for the infusion. Other short-term side effects and cautions (such as avoiding people with infections, not eating unpasteurised cheese etc) are minimal, although I did find myself very susceptible to colds immediately following treatment, some of which were long-lasting and quite unpleasant!

On-going monitoring
Because of possibility of developing other autoimmune conditions, the patient must be monitored for at least three years using blood tests.

**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;

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

- 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

**N/A**

**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.

At the moment, Alemtuzumab has only been available to a small cohort of MS-ers through clinical trials. As these have now closed, the treatment is currently unavailable to patients as part of routine care and so I cannot comment on whether there would be any differences between the care and treatment offered through clinical trial research and normal NHS care.

However, I have been a member of an online social network for patients (Patientslikeme) since 2008, where both MS and the various treatments offered for it globally are frequently discussed. Other patients in the US who have received treatment with Alemtuzumab have reported their own experiences of their condition, treatment and on-going health which match my own experience as reported to the MS Society for their statement and in this personal statement.

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

As stated above, this treatment is not offered currently under normal NHS care. Perhaps the only potentially adverse issue that I would mention to an MS-er hoping for treatment is the requirement for on-going blood tests to monitor the re-population of the immune system and to check for development of other auto-immune conditions such as thyroid or kidney conditions (Hashimoto's disease or Goodpasture's disease) or thrombocytopenic purpura. Given that these blood tests are in the patient's interest to give early warning of such emerging conditions and allow treatment, they are a bit inconvenient but obviously very necessary!

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.

**Availability of this technology to patients in the NHS**

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

Alemtuzumab offers a new paradigm in the treatment and care of people with MS. If this drug was licenced for use in the NHS, it holds out hope for those with relapsing-remitting MS to have a treatment (over two years, with two infusions) that would 'future-proof' them against developing more serious MS later in life, suffering high levels of relapses and eventually ending up with MS acquired disability that seriously impacts on their life, their work prospects, their family and friends and the welfare and social care sector. If offered as a 'first treatment', especially to the newly diagnosed, it has the potential to drastically reduce the numbers of people with MS who progress on to more serious forms of the disease. With a greater proportion of the MS population offered treatment with Alemtuzumab as NHS inpatients, more of them would be likely to continue working for longer, maintain their independence for longer and be less likely to become reliant on carers - and so the benefit is far more wide-reaching than just the person treated; carers (usually family in the first instance) would also benefit alongside the patient. I may sound like an advert for the drug, but I firmly believe that it is the best thing that has happened to my MS, me and my friends and family. Without this treatment I am scared to think how bad my MS might have become or where I would be now. People I have had contact with through the online community say similar things – to the extent that many of us now feel like 'ex-MSers'.

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

Although there are DMDs currently available on the NHS, none of them offer the same hope to patients as Alemtuzumab. Patient forums where injectable DMDs are discussed are full of stories of the dread that people feel ahead of their next injection and the difficulties many people face with injecting themselves (often coming to rely on a family member to do the deed instead) – and of the side-effects they suffer post-injection. Having to inject their drug of choice on a regular basis often becomes too much for them to bear and many cease treatment after a handful of years. Alemtuzumab may indeed have a higher 'up front' inconvenience and side-effect factor, but once the treatment is over, it is done, allowing the patient to continue with a normal life. While the recent development of a daily oral pill is a huge step forward, the decreased rate of relapse reduction and disability acquisition is much better with Alemtuzumab, and does not rely on adherence to taking a pill daily. No other current treatment offers the long-term benefits of Alemtuzumab, and if this drug is not licenced, people with MS will continue to suffer.

Are there groups of patients that have difficulties using the technology?
None, as far as I know (of those groups that are eligible for treatment with Alemtuzumab – i.e. those with RRMS).

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal (STA)

**Other Issues**

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

Based on my own personal experience and reported experience in discussions on patient forums, the provision of care to people diagnosed with MS is patchy and generally poor. Many people are diagnosed with MS and then never offered treatment at all; many are not even able to see an MS nurse for 'supportive care', and there is a lack of specialist MS clinics in hospitals and general understanding of MS by GPs in practice. Although injectable forms of DMDs and the new daily pill are licensed, the proportion of people diagnosed with MS receiving such treatments is low. If Alemtuzumab were to be licensed it would put a new treatment onto the market that has proven long-lasting beneficial effects that requires only a couple of inpatient visits to hospital to administer and in the long run makes good economic sense, balancing cost against beneficial outcomes.