Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly.

The Appraisal Committee is interested in receiving comments on the following:

- has all of the relevant evidence been taken into account?
- are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- are the provisional recommendations sound and a suitable basis for guidance to the NHS?

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 the preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations:

- could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced.

| Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank): | MS Society |
|Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry. | None. |
|Name of commentator person completing form: | Jack Doughty |
Beta interferon and glatiramer acetate for treating multiple sclerosis (review of TA32) [ID809]

Consultation on the appraisal consultation document – deadline for comments end of 24 January 2018

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Do not paste other tables into this table, because your comments could get lost – type directly into this table. |
| Example 1      | We are concerned that this recommendation may imply that …………… |

1 Summary

We are concerned that the recommendation to restrict the number of treatments used as first line therapies could have a detrimental impact on the lives of people with MS. While we acknowledge that all of the treatments appraised are similarly effective, there are important reasons why people with relapsing MS prefer different beta interferons or glatiramer acetate over Extavia. These include a variety of reasons unrelated to efficacy but nevertheless important in ensuring people start and remain on a treatment. Reasons include mode of delivery and ease of use, side effects, storage requirements, impact on daily life and whether they are planning to start a family. Limiting the range of beta interferons and glatiramer acetate to Extavia only is likely to increase the chances of people choosing not to take any treatment at all and in turn experiencing potentially avoidable relapses and disease progression. Less people managing their MS as well as they would otherwise would will mean a greater burden on wider NHS services and carers.

“All MSers should have a treatment choice. It’s universally accepted that no two patients experience the same symptoms, there is no reason to expect that one treatment option can fit all sizes.” – Person with MS

As MS affects everyone differently people find that different treatments are better suited to their MS. Beta interferons and glatiramer acetate have been used for years as the first line treatment when taking an escalation therapy approach to treating MS. The current ABN guidelines state MS specialists may adopt an escalation approach, starting patients on a less toxic drug and only switching if this does not control their disease. Limiting the number of less toxic treatment options will result in more people choosing not to start any treatment.

While many people with MS are currently taking beta interferons or glatiramer acetate, Extavia has been one of the least prescribed options within this category. The low prescribing rate of Extavia is likely due to the fact that people with MS generally choose to take one of the other treatments looked at within this appraisal.

2 Impact on people who’ve experienced single clinical episode

Under these recommended changes, people who have experienced a single clinical episode with multiple MRI lesions (regardless of whether they have had an MS diagnosis or not) will have their treatment options severely limited.

These recommendations would mean that people diagnosed with MS who have had only one clinical episode with MRI activity will now only have the option of taking Extavia or alemtuzumab.

As acknowledged in the DMT algorithm, alemtuzumab is unlikely to be prescribed for someone who has only experienced one clinical episode, so in practice people who’ve experienced one relapse will only be eligible for Extavia and will have no option to switch to another beta interferon if they

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experience negative side effects while taking Extavia. Those people, who would have preferred to take a different beta interferon over Extavia, due to a reason other than its clinical efficacy, will most likely choose to go without treatment. This would mean a delay in starting a treatment until they have another clinical episode and therefore qualify for a greater number of treatments. This would risk their MS progressing faster than it would have if they had a wider range of first line treatment options. This recommendation would unfairly impact on this subgroup of people with MS who would have their options severely limited.

3 Safety profile of beta interferons and glatiramer acetate

Though less effective than some of the newer treatments now available, beta interferons and glatiramer acetate are an important option for pwMS. They offer people who are less inclined to take risks a treatment option with a reliable safety record and proven efficacy. This is a particularly important option as within MS DMTs, the general rule is that the higher the efficacy of the treatments, the greater the risk of side effects. The greater the range of DMTs available means that more people are likely to find the treatment that suits them. If these DMTs were no longer available on the NHS, it could result in less people being effectively treated for their MS.

The Association of British Neurologists (ABN) specifically recommends beta interferons and glatiramer acetate for ‘individuals with relatively quiescent disease’. They also highlight the safety profile of these DMTs, which have been available on the NHS through the RSS since 2002, as meaning they provide an effective treatment for the ‘more risk averse’. This has been backed up by case studies gathered by the MS Society (to inform our previous submission to the MTA); several people commented on feeling most comfortable with the known risks of the more established DMTs opposed to newer, riskier DMTs.

Research into the tolerance of pwMS to take risks with DMTs has found that 15-23% of respondents were not willing to take any risk for their MS therapy. This study found the factors such as gender, age, disability and information seeking behaviour influenced risk tolerance. It is important that pwMS continue to be able to access beta interferons and glatiramer acetate as they represent treatment choices where there is a known safety record.

4 Mode of Delivery

The reasons different people choose to take one treatment over another are diverse and not just related to the clinical efficacy of each treatment. One of the strongest influences on why someone chooses one treatment over another is mode of delivery.

When given a choice to take one of the beta interferons or glatiramer acetate, a number of people with MS have told us that the reason they chose their treatment was because it was administered less frequently. People particularly mentioned choosing Avonex because it is administered once a week, and Plegridy because it is administered fortnightly. This means that they spend less time having to think about treatment, less time self-injecting and less time dealing with side effects. As one person who has been taking Avonex for years commented:

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3 Fox et al, Risk tolerance to MS therapies: survey results from the NARCOMS registry, Mult Scler Relat Disord. 4(3):241-9, May 2015
"In the absence of any other information or reassurances from NICE that the side effects of Extavia do not last anything like as long as those from Avonex, then their recommendation is more or less restricting some future patients to an interferon treatment that leaves them substantially impaired for most of the time."

On the other hand, some people with MS who experience cognitive issues have told us they chose a treatment which is taken more frequently as they find it easier to remember and keep to the schedule. This reflects the variation in why people with MS choose different treatments.

Another mode of delivery factor that many people with MS have commented on as an influence when choosing a treatment is the pre-filled ‘straight forward pen device’ which many are self-administered with, including Rebif, Plegridy and Avonex. These developments in how the DMTs are administered show that improvements are being made to reduce the side effects and ease of use.

One factor that dissuades many from choosing Extavia is that it comes in a powder form that the patient has to mix before administering, with a 44 page instruction pack Extavia is clearly not the simplest beta interferon to self-administer. For people who have problems with dexterity or cognitive issues, the complicated process for taking Extavia can be extremely off putting. Without the option of easier to take treatments, many people with MS would likely need more support from a carer to help administer Extavia.

Diversity of choice in treatments offered by the NHS means that pwMS are more likely to find the DMT which best suits their condition and lifestyle. This contributes to the overall cost effectiveness of MS on the NHS and wider support services as more people on DMTs results in less relapses and slower disease progression.

### Side effects

The side effects that each beta interferon and glatiramer acetate come with play a big role in influencing why someone opts for one drug over another as well as why many people switch from one to another. Side effects of beta interferons include flu like symptoms which people experience after injecting as well as unpleasant injection site reactions which lead some people to develop needle phobia.

A number of people have told us that they chose Copaxone as their treatment option when they were first diagnosed as they were informed it had fewer side effects than the beta interferons.

We have also heard from people who are concerned that they will not be allowed to continue with their treatment if, due to issues such as thyroid problems, they are required to take a break. One person commented “taking any of these drugs is stressful enough without having the extra stress of removing what may have been the only drug which worked for my body”.

Only having the option of Extavia would likely result in many people who experience side effects having little other treatment options. This was the case with one person who told us that they had only been offered Extavia due to their MS nurse telling them it was the cheapest option and that they would only be considered for another option if Extavia proved ineffective. Not given a role in deciding which treatment they would prefer, this person had a negative experience with Extavia due to side effects, commenting: “It made me feel worse, more dizzy etc so only lasted 3 months on it. A neurologist even thought I was suicidal when I said I felt better having nothing than that injection”.

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In paragraph 3.2 the committee highlights that ‘its remit was to revisit the original appraisal, and to compare to beta interferons and glatiramer acetate with best supportive care, rather than the newer drugs’. However, in paragraph 3.25 the committee reports that while the treatments may be considered innovative compared with best supportive care, they are not when compared to the newer treatment options and therefore should not be considered innovative. This argument seems to go directly against the parameters guiding this appraisal. When compared to best supportive care, all of the treatments under appraisal should be considered innovative.

Currently Copaxone is the only licensed treatment for relapsing MS which is not contraindicated for pregnancy and is often chosen by women who are planning to start a family. The argument put forward in the appraisal consultation document that ‘special considerations’ shouldn’t be applied for Copaxone due to the marketing authorisation suggesting that it is preferable to avoid taking during pregnancy ignores the evidence from both people with MS and their clinicians.

We have heard from neurologists who have expressed particular concern over this aspect of the recommendation highlighting that they regularly prescribe Copaxone to women who are planning a pregnancy as the risk of not taking a treatment at all outweighs the risks involved in taking Copaxone while pregnant. As it is not contraindicated in pregnancy, the judgement on the risk involved, is down to women with MS and their neurologist, the committee should not be making this judgement on their behalf. NICE should listen to the judgement of neurologists who regularly make decisions with their patients on whether Copaxone is safe to take when pregnant and breastfeeding.

We have been contacted by women who plan to switch from treatments such as dimethyl fumarate to Copaxone while they try to start a family. The committee’s recommendation that Copaxone does not deserve special consideration goes directly against Copaxone’s licence and general prescribing practice in England and Wales and should be reconsidered.

The appraisal consultation document makes no mention of the extra support given by some of the pharmaceutical companies to help people take their products. If Extavia is the only option for new patients we would want to see that they are given the same level of support that those who are already taking one of the other beta interferons receive. While Extavia may be the most cost effective option does this factor in the 24 hour nurse support phone number that some of the other treatments provide?

Lifestyle factors for people with MS are often a big reason why they choose one treatment over another. The storage requirements of these different treatments mean that people find one is a better fit around their daily life. For example a cold chain is less essential when taking Pledigrdy, which makes it a more practical choice for people who need to travel a lot such as people with MS who...
serve in the military. More frequent injections that need to be stored in a refrigerator make it difficult for people to travel. A number of people have commented to us that they simply stopped going abroad while taking beta interferons as they found it too much hassle.

Compared to many of the treatments approved more recently by NICE, beta interferons and glatiramer acetate have less burdensome monitoring requirements, with 6 monthly blood tests for the former and none for the latter. This can be a factor in why people choose one of these treatments:

“I still work, I cannot afford to be off work with side effects of some of the other medication. I didn’t want to have to attend regular blood tests as required for some drugs I had a choice of. I felt that with the minimal effect on my body that this medication would suit me best.”

10 Impact on newer appraisals

We would like to see some consideration over what impact this could have on the appraisals which have taken place since 2002 which have used beta interferons and glatiramer acetate as a comparator. Would newer appraisals have to go to reappraisal? This would cause a great level of concern for people with MS currently on these treatments.

11 Lack of transparency

We do not feel that the basis for this decision has been transparent. The recommendation of the appraisal consultation document sees all of the treatments as of a similar efficacy, and therefore base’s its decision on the cost effectiveness of each option. As cost effective analysis is not provided within the document we are unable to make an argument as to whether more treatments than Extavia are cost effective. The discussions with pharmaceutical companies over the price of their products have also not happened in the public domain and we are unable to scrutinise these decisions.

While the risk sharing scheme has been used as the key data for this appraisal, the final results are still yet to be published, this is another reason why the decision to provide Extavia alone is not as transparent as it should be. It is unclear to us why NICE and the Department of Heath have not made this data available to the public and we would like to know why this decision has been made.

12 These recommendations will also unfairly impact on people who:

- Have a history of seizures and shouldn’t be offered beta interferon but can be offered glatiramer acetate
- Are unable to swallow tablets and will have their first line treatment range reduced to Extavia and Alemtuzumab only.

14 We would also like to know how this recommendation would impact people who are currently taking one of the restricted treatments but are required to have a break for some reason. Would they be required to start Extavia instead despite having been taking one of the other options previously?

Insert extra rows as needed

Checklist for submitting comments

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- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in turquoise and all information submitted under 'academic in confidence' in yellow. If confidential information is submitted, please also send a 2nd version of your comment with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the Guide to the processes of technology appraisal (section 3.1.23 to 3.1.29) for more.
Consultation on the appraisal consultation document – deadline for comments end of 24 January 2018

- Do not include medical information about yourself or another person from which you or the person could be identified.
- Do not use abbreviations. Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.
- If you have received agreement from NICE to submit additional evidence with your comments on the appraisal consultation document, please submit these separately.

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