

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

<p>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:</p> <ul style="list-style-type: none"> • 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? <p>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:</p> <ul style="list-style-type: none"> • 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. <p>Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced.</p>	
<p>Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):</p>	<p>[Multiple Sclerosis Trust]</p>
<p>Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.</p>	<p>[None]</p>
<p>Name of commentator person completing form:</p>	<p>[Janice Sykes, Information Management Officer]</p>
<p>Comment number</p>	<p style="text-align: center;">Comments</p> <p style="text-align: center;">Insert each comment in a new row.</p>

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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	<p>Summary</p> <p>We strongly believe that all current treatments should remain available as a treatment option for all eligible patients.</p> <ul style="list-style-type: none"> We consider that the proposal to recommend Extavia alone is discriminatory towards those for whom problems with dexterity, vision and cognition form part of their disability (see 3.1). We consider that the proposal to recommend Extavia alone is discriminatory towards women of childbearing age who intend to conceive, as it will remove all appropriate treatment options (see 3.6). <p>This decision has been made without reference to clinical practice or experience and ignores significant real-world differences between each of the beta interferons and glatiramer acetate. We are particularly disappointed that this recommendation does not acknowledge individuality and would take away choice from people with MS.</p> <p>NICE has acknowledged that all six drugs are equally effective at reducing the number of relapses and slowing down disability progression. The decision to approve Extavia and not the other five drugs is based on the cost of the drugs; Copaxone and the other beta interferons are more expensive than Extavia.</p> <p>No consideration has been taken of the potential impacts on people with MS and on specialist MS services or the costs of these impacts.</p> <p>The MS Trust's expertise lies in understanding and representing the perspectives of people with MS and ensuring that people have access to effective treatments.</p> <p>We invited comments on the ACD from people affected by MS and from health professionals. Over 500 people with MS and over 100 specialist MS health professionals (26 neurologists, 73 MS specialist nurses, 5 MS specialist therapists, 4 pharmacists) responded to our survey; their feedback has informed our response to the ACD and is provided in the appendices to this document.</p> <p>In both surveys, 98% of respondents disagreed with the NICE recommendations, and many gave explicit examples to explain their response. We urge you to look at our supporting appendices to see what people with MS and specialist MS health professionals have said about the recommendations.</p>
2	<p>Importance of beta interferons and glatiramer acetate in the current treatment pathway</p> <p>Because of the unique circumstances of this multiple technology appraisal, the committee is in the position of appraising six drugs which have been prescribed by the NHS for more than fifteen years. The drugs are established treatments with well-defined safety profiles. MS teams are very experienced with these agents; there is a wealth of published research and clinical experience confirming their general safety; there are well-established services to initiate and monitor</p>

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

	<p>treatment. Despite the availability of alternative oral treatments since 2014, the beta interferons and glatiramer acetate continue to be prescribed widely.</p> <p>Extensive real-world experience of these agents has confirmed that at an individual patient level, different products suit different individuals. There are significant differences between the drugs in terms of ease of use, dosing schedules, storage, side effects, safety during pregnancy and tolerability. These factors impact on different people to a greater or lesser extent, and individuals will have personal preferences which enable them to effectively manage their treatment. The availability of a range of treatment options accommodates the widest possible range of patient and clinician preferences, enhances patient adherence and, consequently, clinical effectiveness.</p> <p>Shared decision making is a priority for the NHS and has become an important component of helping patients to choose the disease modifying drug which is right for them. Approving Extavia alone and withdrawing the remaining beta interferons and glatiramer acetate will severely limit the potential for MS teams to share the decision process and find a treatment that is right for the individual and their circumstances.</p> <p>The beta interferons and glatiramer acetate are of particular benefit to those who are risk-averse and those who have a relatively low MS activity¹; for many people, their MS has remained stable while taking one of these drugs. We are aware that some people who switched from one of the injectable drugs to an oral treatment have subsequently switched back to an injectable drug; others who have started with one of the oral treatments have experienced side effects and switched to one of the beta interferons or glatiramer acetate.</p> <p>The impact on patient care of approving Extavia alone and withdrawing the remaining beta interferons and glatiramer acetate should not be overlooked.</p> <p>Our comments focus on the following major issues:</p> <ul style="list-style-type: none"> • impact on people with relapsing MS • impact on MS services • overarching criticisms of the appraisal
<p>3</p>	<p>Impact on people with relapsing MS</p> <p>The differences between each of the beta interferons and glatiramer acetate have a significant impact on people with MS, this has not been taken into account by NICE in reaching this decision. In pooling the data from the RSS, which excluded Extavia, the differences between the drugs was not apparent; yet the impact of this real-world difference on patient adherence should not be overlooked. Dosing schedules, storage, side-effects and tolerability vary greatly between the drugs and we have reports of people who have had bad experiences on a particular drug, which leads to non-adherence.</p> <p>Non-adherence on a particular drug because of a bad experience, can also lead to disillusionment with MS treatments in general. Evidence demonstrating the value of treating people with MS early is compelling, and therefore if people refuse treatments this can lead to poorer health outcomes and increased disability, which increase the demand for services and therefore costs to the NHS.</p> <p>Our own research and that of the MS Society shows that Extavia is the least prescribed of the six modifying drugs under consideration². In our HP survey, 11% of respondents commented that all</p>

¹ Scolding N, et al. Association of British Neurologists: revised (2015) guidelines for prescribing disease-modifying treatments in multiple sclerosis. Practical Neurology 2015;15(4):273-279.

² MS Trust. Evidence for MS specialists: findings from GEMSS. Letchworth: MS Trust; 2016
MS Society. My MS, My Needs 2016: access to treatment and health care. London: MS Society; 2016

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

	<p>treatments except Extavia were offered by their MS team; 9% of respondents commented that Extavia was offered as an option but no one on their caseload was taking it. In our survey of people with MS, just 0.4% (2/522) indicated that they had taken Extavia. Particular issues around ease of use, injection frequency and other factors are explored below, demonstrating why this is the least preferred of the options.</p>
<p>3.1</p>	<p>Ease of use</p> <p>We consider that the proposal to recommend Extavia alone is discriminatory towards those for whom problems with dexterity, vision and cognition form part of their disability.</p> <p>All of the drugs under evaluation, with the exception of Extavia and Betaferon, are provided as ready-to-use injection devices.</p> <p>Extavia is supplied as solvent and powder which must be made up each time it is taken. The Patient Information Leaflet for Extavia details the seventeen step instructions for doing this: www.medicines.org.uk/emc/files/pil.6529.pdf. For the MS Decisions resource we prepared a video which shows how the injection is made up https://youtu.be/bxyMMa2vNHA and injected https://www.youtube.com/watch?v=Q0_RopyN66w.</p> <p>People with manual dexterity, visual or cognitive difficulties, all of which are common problems in MS, will find this very difficult, if not impossible, to do. Those with fatigue or busy lives will also struggle to make up and inject Extavia every other day.</p> <p>13% (70/522) people with MS responding to our survey mentioned ease of use as a major criteria for choosing an injectable disease modifying drug.</p> <p>People with MS: <i>They should try mixing Extavia with gloves on. Hopefully they will realise how difficult it can be for people with reduced dexterity due to lack of sensation in finger tips.</i></p> <p><i>Smaller needle albeit three times a week, came already filled, I could and still self-inject especially as I have dexterity issues meant didn't have to faff about and do it myself swiftly and easily. Still the case as I live by myself.</i></p> <p><i>I take Avonex and chose this drug because you inject with an easy to use pen once a week.</i></p> <p>MS specialist: <i>In my experience Extavia is not often chosen due to the difficulties in making it up, the dexterity required and those with fatigue and busy lives aren't able to cope with this every other day.</i></p>
<p>3.2</p>	<p>Injection frequency</p> <p>The drugs under evaluation are self-injected at different intervals, from daily to once a fortnight. Injection frequency is one of the most important factors in treatment choice, with daily, weekly or fortnightly frequencies being most popular.</p> <p>Extavia is injected every other day, a pattern that is not easily remembered. Over a two week period, patients are injecting on a different day of the week, which increases the risk of simply forgetting to do an injection and consequently losing therapeutic effect. Ultimately, it increases the risk of relapses, of someone discontinuing treatment altogether and in the longer term acquiring greater disability due to relapses or progression.</p>

Beta interferon and glatiramer acetate for treating multiple sclerosis (review of TA32) [ID809]

NICE National Institute for Health and Care Excellence

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

	<p>More frequent injections lead to a higher incidence of injection site reactions, increasing the need for hospital visits to deal with infected injection sites and increasing the risk of discontinuing treatment. Patients are instructed to rotate injection sites; with less frequent injections, there is more opportunity for an injection site to recover before it is used again.</p> <p>20% (103/522) people with MS responding to our survey mentioned injection frequency as a major criteria for choosing an injectable disease modifying drug.</p> <p>People with MS: <i>Only having to manage the injection every two weeks means that any side effects are limited to every other weekend and have not impacted on my ability to work full time.</i></p> <p><i>I chose Avonex initially as injection was weekly and the least invasive to my life. The same decision I made when swapping to Plegridy which was a fortnightly injection.</i></p> <p><i>I am considering Plegridy as it is once a fortnight and the side effects appear manageable.</i></p> <p>MS specialists: <i>In my experience Extavia is not often chosen due to the difficulties in making it up, the dexterity required and those with fatigue and busy lives aren't able to cope with this every other day.</i></p> <p><i>People choose the other injectables for a variety of reasons e.g. less frequent injections.</i></p> <p><i>Extavia has the same efficacy as the other injectables, but is not chosen by people with MS as it is difficult to remember to take it being on alternate days. We now have more people on Plegridy and Copaxone. The former because of the less frequent administration and the latter due to its lack of side effects profile.</i></p>
3.3	<p>Side effects</p> <p>People often experience flu-like symptoms after each beta interferon injection. These can be severe and are a major reason why people stop taking one of these drugs. Every other day injections required for Extavia make it particularly difficult to manage the impact of flu-like symptoms on work and family life; less frequent dosing schedules such as weekly or fortnightly make it possible to plan injections at a time (for example over the weekend) when flu-like symptoms will have less impact.</p> <p>Glatiramer acetate does not cause flu-like symptoms and is often a preferred option for this reason.</p> <p>Other disease modifying drugs are associated with side effects which are a significant concern for some and influence choices made by neurologists and patients. Dimethyl fumarate carries the risk of a serious brain infection, alemtuzumab leads to thyroid problems and there is an increased risk of birth defects in women taking teriflunomide. Some side effects make drugs unsuitable for people with pre-existing conditions, for example gastrointestinal side effects make dimethyl fumarate unsuitable for people with gastritis or inflammatory bowel syndrome.</p> <p>The severely restricted list of drugs that would be available as a result of this ACD will make it much more difficult for MS specialists and patients to choose a suitable treatment based on side effect profile, either at treatment initiation or, more importantly, treatment switching.</p> <p>People with MS: <i>Extavia worked fine until I was too bruised and skin hardened so injection liquid started coming out again. Switched to Tecfidera, but am having problems with side effects still after half a year, so don't know what to switch to now.</i></p>

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

	<p><i>Copaxone, despite having one possible nasty side effect, appealed to me because it would not leave me with flu-like symptoms and needing to take additional medication to combat it.</i></p> <p><i>Based on thinking through options available chose Copaxone as it did not cause flu symptoms on injection days.</i></p> <p><i>I felt flu like side effects during the night of administration, and sometimes the next day, which is frustrating, but it is ok as it is only one day per week.</i></p> <p><i>Didn't want side effects from meds daily.</i></p> <p><i>Rebif was one of the less "invasive" drugs - by that I mean the side effects were less serious than that of stronger drugs such as Tecfidera. Plus, it was recommended by my neurologist. As I had a low white blood cell count and digestion issues we felt Copaxone would be the best drug for me.</i></p> <p>MS specialists: <i>I can foresee patients having to transfer onto a more expensive drug after failing on Extavia rather than trying an alternative injectable. They will then be forced to choose one of the oral drugs and accept their associated risks and monitoring even if this impacts upon their daily life and causes anxiety regarding possible severe side effects.</i></p> <p><i>The side effects should be considered - an injection of interferon every other day is less tolerated than an injection every two weeks or glatiramer acetate every day. Cost-effectiveness should include the costs of managing side effects and the effect of side effects on employment.</i></p>
3.4	<p>Severely limited choice</p> <p>With this recommendation, NICE is proposing that treatments available to people with active relapsing MS would be: interferon beta 1b (Extavia), teriflunomide (Aubagio), dimethyl fumarate (Tecfidera) and alemtuzumab (Lemtrada).</p> <p>Teriflunomide, dimethyl fumarate and alemtuzumab are each associated with side effects which may make them unsuitable, particularly for those with comorbidities or those who are risk averse. People taking one of these first line treatments may experience an adverse event such as liver injury or prolonged lymphopenia and be unable to continue taking the drug. They will have greatly limited choice if Extavia is the only injectable treatment available to them, with the risk that they may not take up or may discontinue treatment entirely.</p> <p>16% (82/522) people with MS responding to our survey raised the issue of severely limited options if Extavia was the only injectable disease modifying drug.</p> <p>26% of health professionals responding to our survey specified concerns that the decision limited patient options.</p> <p>MS specialists: <i>People who require first line treatment and cannot tolerate the oral medications will have limited options.</i></p> <p><i>Limited choice. Extavia is more difficult to tolerate than some of the other injectables.</i></p>
3.5	<p>Drug safety monitoring</p>

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

	<p>The proposed first-line treatments require more frequent blood and urine tests to monitor for potential side effects. For many people, this will mean a visit to a hospital clinic which is often disruptive for family and work commitments and can involve significant travel costs. Glatiramer acetate is often preferred as no safety monitoring is required. This minimises the impact of the treatment on family and work commitments. In addition, the focus of health professionals to manage the increased monitoring requirements impacts on people with MS who may have to wait longer for review appointments or when experiencing a relapse.</p> <p>2% (9/522) people with MS specifically cited lack of monitoring on Copaxone as reason for choice</p> <p>People with MS: <i>It [Copaxone] suited my lifestyle. No monitoring, wouldn't get in way of my job.</i></p> <p><i>I chose Copaxone because I was in full time work and it was simple, no significant side effects and no need to take time off work for blood tests.</i></p>
3.6	<p>Use of treatments during conception and pregnancy</p> <p>We consider that the proposal to recommend Extavia alone is discriminatory towards women of childbearing age who intend to conceive, as it will remove all appropriate treatment options.</p> <p>The committee rejected equality considerations concerning safety of glatiramer acetate during pregnancy based on the wording of the marketing authorisation. The committee will be well aware that the wording used is routinely hypercautious. There is now substantial data to show that glatiramer acetate can be taken safely during pregnancy, reflected by the fact that this is now well-established in clinical practice. As noted by a neurologist responding to our survey: "The exclusion of Copaxone would be a particular loss to women wanting a safe disease modifying drug during pregnancy - for which this drug is now routinely used in some centres."</p> <p>The proposed first-line treatments Extavia, teriflunomide, dimethyl fumarate and alemtuzumab all carry significant risks during pregnancy and are contraindicated.</p> <p>3% (14/522) people with MS responding to our survey raised the issue of conception and pregnancy as a consideration when choosing an injectable disease modifying drug.</p> <p>17% (20/122) of HPs responding to our survey raised the issue of conception and pregnancy as a consideration when choosing an injectable disease modifying drug.</p> <p>People with MS: <i>First of all, the worst decision would be rejecting Copaxone. As far as I know it is the only drug for people with not very active MS that can be taken while pregnant or breastfeeding.</i></p> <p><i>Upset. I want to start a family and the only drug that has been moderately approved for pregnancy is Copaxone. To remove that drug takes away my decision between possible permanent disability or starting a family.</i></p> <p>MS specialists: <i>These recommendations are a harmful retrograde step in the management of patients with MS. They completely remove from patients the ONLY licensed treatment with evidence of safety during pregnancy (copaxone). Because of this I consider the recommendation to be discriminatory on the grounds of gender.</i></p>
4	Impact on MS services

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

<p>4.1</p>	<p>Greater costs for NHS and social care systems</p> <p>Many people are not happy with the higher risks and possible side-effects associated with the proposed first-line treatments for relapsing MS. Faced with a choice between frequent injections and the flu-like side effects of Extavia and the higher risk side effects of these treatments, many people will choose no treatment. This is likely to lead to increased burdens on the NHS due to the more rapid progression of MS – e.g. more GP and consultant appointments; more time needed with specialist nurses; greater pressure on social care and family care systems; more unplanned hospital admissions etc.</p> <p>MS specialists: <i>Limiting the options to one drug is likely to limit uptake of treatment at this stage, which may have implications for future disease activity and disability.</i></p> <p><i>It may result in short term savings but is likely to increase long term costs with treatment failure and escalation.</i></p> <p><i>Absolutely shocking decision that will cause disabling and distressing relapses resulting in an increase in the need for symptom management, rehab, social care and benefits.</i></p>
<p>4.2</p>	<p>Patient care</p> <p>People who struggle with manual dexterity, visual or cognitive issues will require additional support from MS services to manage their treatment.</p> <p>In addition, the drug monitoring requirements of the proposed alternatives impact on the health professionals who support people with MS. The time taken to carry out the higher level of monitoring will increase the pressure on an already overstretched workforce. As a result, other patients may have to wait longer for appointments or the costs of additional staff to manage the workload will be incurred.</p> <p>MS specialists: <i>More clinic time for reviewing and possible administration due to poor dexterity.</i></p> <p><i>We would get an increase in calls, patient visits and a lot of complaints.</i></p>
<p>4.3</p>	<p>Lack of Patient Support Programme</p> <p>Extavia has a very limited patient support programme. This will put extra pressure on the MS nurses to train people when they start injecting and support them when they have problems with side effects or injection technique.</p> <p>MS specialists: <i>Many patients cannot do this [make up treatment] and cannot rely on others to do it. I am sure that GP services would be unable to accommodate alt[ernative] day injections being administered, nor could the district nursing teams. Within MS we teach a self-management approach to wellbeing and the choice of drugs has been an integral part of this, it helps with adherence to medication, I truly believe that we reduce wasted medication costs to the NHS when taking into account choice of DMD.</i></p> <p><i>They would not get the support that the other drug companies offer (nurse support package).</i></p>

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

	<p><i>Novartis DO NOT provide training demo kits for patients any more. So we cannot train our patients!</i></p> <p><i>If Extavia became the only therapy option for RRMS, we would be unable to continue supporting patients at home with Injection training and follow on support and care. This would have a huge impact on the MS Specialist Nurses who would then have to train all patients in their clinics resulting in a huge increase in their already overburdened workloads.</i></p>
4.4	<p>Increased demand for oral treatments</p> <p>The decision to recommend Extavia alone will increase demand for teriflunomide, dimethyl fumarate and alemtuzumab. This will place increased pressure on over-stretched services in order to initiate treatment, provide side effect management and drug safety monitoring.</p> <p>MS specialists: <i>I can foresee patients having to transfer onto a more expensive drug after failing on Extavia rather than trying an alternative injectable. They will then be forced to choose one of the oral drugs and accept their associated risks and monitoring even if this impacts upon their daily life and causes anxiety regarding possible severe side effects.</i></p>
4.5	<p>Management of patient expectations</p> <p>Specialist MS teams will need to deal with the problem of treating patients who will be offered different treatments according to the date their MS was diagnosed which will add to the complexity of managing disease modifying drugs within the MS service. Health professionals will need to explain the lack of treatment options to newly diagnosed patients, placing them in potentially upsetting and difficult positions and ultimately leading to increased pressure on services. It may also lead to lower staff morale, as specialist teams will be unable to offer what they consider as better or more appropriate treatment options, and will be unable to provide high standards of care due to increased workload.</p> <p>MS specialists: <i>I think many MS people would be unhappy due to side effects etc., and would be calling in for assessment and advice which would ramp up pressure to our already stretched out services.</i></p> <p><i>I feel this is very poor judgement on NICE's part. By limiting the options to patients you are causing wider problems in the long term. NICE continually recommends treating patients as individuals and tailoring their care to them then proceeds to offer a 'one treatment fits all' approach. This WILL have a negative impact on drug compliance, reduce patients' options when they have a reaction to extavia and put over-whelming pressure on a delivery service that already messes up orders.</i></p> <p><i>Medications that are already a reminder of having MS need to fit in as seamlessly as possible with someone's life for them to feel comfortable with it, for them to be accepting of side effects and for them to stick with it. I think there are very likely to be more switches to other treatments and therefore ultimately cause disruptions to patients and add to the workloads of already stretched services.</i></p> <p><i>The most important thing is being able to offer people with MS choice of treatments so as we can work collaboratively to find the most effective treatment that they can tolerate, administer with least effort and minimal if any side effects. We can only do this if we have the range available.</i></p>
5	Overarching criticisms of the appraisal
5.1	Lack of transparency

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

	<p>The proposal to recommend Extavia alone is based on cost-effectiveness. However, as the ACD states, the drug costs are 'commercial in confidence'. This means that stakeholders and members of the public are not able to evaluate the most important issue governing the Committee's decision to approve Extavia and reject the remaining five drugs.</p> <p>It is also unclear to what extent the manufacturers have been able to participate in negotiations over patient access schemes and discounts. None of these discussions have been conducted in the public domain.</p>
5.2	<p>Best supportive care</p> <p>NICE has compared the cost of the beta interferons and glatiramer acetate with best supportive care, and found Extavia alone is cost effective. No details are given of what would constitute "best supportive care". The MS Trust and other stakeholders have raised the issue of best supportive care as a comparator in previous single technology appraisals: it has been rejected as a comparator because (1) it is not an option in current clinical practice, (2) the concept is idealistic because in reality people with MS often have very limited access to services, (3) there is no consensus on what best supportive care is and how much it costs, and (4) it is inconsistent to compare the cost of a disease modifying drug which has a constant cost regardless of location with a comparator which would vary locally since there is no mechanism to ensure that best supportive is consistently implemented.</p> <p>Moreover, in reality, those people for whom Extavia is not appropriate (for reasons outlined above) would instead be offered either teriflunomide, dimethyl fumarate or alemtuzumab. Assessing the beta interferons and glatiramer acetate against best supportive care may have been appropriate when the original TA32 appraisal was carried out more than fifteen years ago, but the committee will know that the treatment landscape for relapsing MS has moved on dramatically since that time. For the purposes of understanding the true cost to the NHS of decisions made in this appraisal, the drugs should be compared to the current, alternative treatment options people will actually be offered; best supportive care is not one of these.</p> <p>Recent single technology appraisals have acknowledged this new treatment paradigm and have made decisions based on cost effectiveness compared with active treatment (dimethyl fumarate TA320, teriflunomide TA303, alemtuzumab TA312). Comparison with best supportive care unfairly disadvantages beta interferons and glatiramer acetate in this appraisal.</p>
5.3	<p>More costly alternative treatments</p> <p>Those people for whom Extavia is not appropriate would instead be offered one of the other "first line" drugs - either teriflunomide, dimethyl fumarate or alemtuzumab. These drugs are more costly and require more safety monitoring than beta interferons and glatiramer acetate; the net effect of the ACD decision will be greater cost to the NHS.</p>
5.4	<p>Innovation</p> <p>Section 3.2 of the ACD states: The committee understood that its remit was to revisit the original appraisal, and to compare beta interferons and glatiramer acetate with best supportive care, rather than with the newer drugs.</p> <p>Section 3.25 states: The technologies are no longer considered innovative.</p>

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

	<p>By comparing the drugs to best supportive care, the alternative treatment option which applied at the time that TA32 was undertaken, but on the other hand refusing to recognise the innovative nature of the treatments which applied at the time that TA32 was undertaken, the appraisal committee is employing double standards. When compared to best supportive care, all of the treatments under appraisal should be considered innovative.</p> <p>Since TA32 was carried out, both Avonex and Rebif have been reformulated to improve their tolerability and immunogenicity. There have also been significant enhancements in the autoinjectors for these two beta interferons which greatly improve patient adherence and therefore clinical efficacy. Although Plegridy has been included in the review of TA32, it is actually a new product, using pegylation to extend circulating half-life and therefore reduce injection frequency making it an attractive option for patients. Finally, Copaxone has been reformulated to provide an alternative dosing schedule, three times weekly in addition to the daily injection frequency. In contrast, there has been limited development of Betaferon and Extavia. Long-term commitment to developing and improving a product should be considered when making this recommendation.</p>

Insert extra rows as needed

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- 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 information.
- 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.

Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

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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