

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Proposed Health Technology Appraisal

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

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of beta interferon and glatiramer acetate within their marketing authorisation for treating multiple sclerosis.

Background

Multiple sclerosis (MS) is a chronic, neurodegenerative disorder which affects the brain, optic nerves, and spinal cord. It often results in progressive neurological impairment and severe disability. Approximately 100,000 people in the UK have MS, and about 2500 people are newly diagnosed each year.

Relapsing-remitting MS (RRMS) is one clinical form of MS which affects approximately 80% of people at time of diagnosis. It is characterised by periods of remission followed by relapses (which may or may not result in residual disability). Most people with RRMS will develop secondary progressive MS (SPMS). Around 65% of people with RRMS develop SPMS within 15 years of diagnosis. SPMS is characterised by more persistent or gradually increasing disability. Some people with SPMS may still experience relapses. MS has an unpredictable course with variable severity and progression. Symptoms can include pain, disturbance to muscle tone including weakness or spasticity, chronic fatigue, unsteady gait, speech problems, incontinence, visual disturbance and cognitive impairment.

There is currently no cure for MS. Current pharmacological management of MS includes disease-modifying agents to reduce the frequency and severity of relapses and the rate of disease progression. These include beta interferon and glatiramer acetate which are not currently recommended by NICE (technology appraisal guidance 32), but are available in the NHS through a risk-sharing scheme. NICE has recommended dimethyl fumarate, alemtuzumab and teriflunomide as treatment options for RRMS (Technology appraisal guidance 320,312 and 303 respectively). For people with rapidly-evolving severe RRMS, natalizumab is recommended (NICE technology appraisal guidance 127). NICE has recommended fingolimod as an option for the treatment of highly active RRMS in adults who have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon (NICE technology appraisal guidance 254).

At the time of technology appraisal guidance 32, beta interferon and glatiramer acetate were not considered to be cost effective. However, it was

recognised that the data on the long term outcomes of beta interferon and glatiramer acetate were limited. It was agreed by the Department of Health that beta interferon and glatiramer acetate would be made available to patients in the NHS if they entered a risk sharing scheme. The risk sharing scheme required an immediate price reduction (for 3 of the 4 products) and a contribution from the companies to NHS infrastructure costs. In addition, the long term clinical outcomes of patients receiving beta interferon and glatiramer acetate were to be recorded in a registry and the companies making these technologies were to make further price reductions to the NHS if cost effectiveness criteria were not met.

The companies included in the risk sharing scheme were Biogen Idec (Interferon beta 1a, Avonex), Merck (Interferon beta 1a, Rebif), Bayer (Interferon 1b, Betaferon) and Teva/Sanofi (Glatiramer acetate, Copaxone). People who were eligible to enter the risk sharing scheme were people with relapsing remitting MS and people with secondary progressive MS in whom relapses were the dominant feature, who meet the criteria laid down by the Association of British Neurologists in 2001. The risk sharing scheme was designed to run for 10 years and it is now due to end in 2016. The final data from this scheme will be considered in the appraisal.

In this appraisal NICE will appraise beta interferon and glatiramer acetate at their current NHS prices, and using additional data on long-term outcomes from the risk sharing scheme, to determine whether these technologies are now cost effective. To do so, NICE has determined that it needs to appraise these technologies within the context of the original appraisal (Technology Appraisal 32). That is, beta interferon and glatiramer acetate should be compared with best supportive care. Since Technology Appraisal 32 was published another interferon 1b (Extavia, Novartis) and a pegylated interferon beta 1a (Plegridy, Biogen Idec) have been granted marketing authorisations. These technologies were not included in the Risk Sharing Scheme because they were not appraised in Technology Appraisal 32. It has been determined by NICE that it is relevant to include these technologies in this appraisal so that guidance can be issued for all beta interferons currently licensed for MS in the UK. Further active treatments that have been licensed and recommended by NICE (including teriflunomide, fingolimod, natalizumab, alemtuzumab and dimethyl fumarate) will not be considered in this appraisal.

The technologies

Interferon beta 1 a (Avonex, Biogen Idec Ltd) is administered by intramuscular injection. It is indicated for:

- people diagnosed with relapsing multiple sclerosis. In clinical trials, this was characterised by 2 or more acute exacerbations (relapses) in the previous 3 years without evidence of continuous progression between relapses.

- people with a single demyelinating event with an active inflammatory process, if it is severe enough to warrant treatment with intravenous corticosteroids, if alternative diagnoses have been excluded, and if they are determined to be at high risk of developing clinically definite multiple sclerosis.

Interferon beta 1a (Rebif, Merck) is administered by subcutaneous injection. It is indicated for:

- the treatment of relapsing MS. In clinical trials this was characterised by 2 or more acute exacerbations in the previous 2 years

Peginterferon beta 1a (Plegridy, Biogen Idec) is a pegylated interferon beta 1a. It is administered subcutaneously. It is indicated;

- in adult patients for the treatment of relapsing remitting multiple sclerosis.

Interferon beta 1b (Betaferon, Bayer) is administered by subcutaneous injection. It is indicated for:

- patients with a single demyelinating event with an active inflammatory process, if it is severe enough to warrant treatment with intravenous corticosteroids, if alternative diagnoses have been excluded, and if they are determined to be at high risk of developing clinically definite multiple sclerosis.
- Patients with relapsing-remitting multiple sclerosis with 2 or more relapses within the last 2 years
- Patients with secondary progressive multiple sclerosis with active disease, evidenced by relapses.

Interferon beta 1b (Extavia, Novartis) is administered subcutaneously. It is indicated for:

- Patients with a single demyelinating event with an active inflammatory process, if it is severe enough to warrant treatment with intravenous corticosteroids, if alternative diagnoses have been excluded, and if they are determined to be at high risk of developing clinically definite multiple sclerosis
- Patients with relapsing remitting multiple sclerosis and 2 or more relapses within the last 2 years
- Patients with secondary progressive multiple sclerosis with active disease, evidenced by relapses

Glatiramer acetate (Copaxone, Teva Pharmaceuticals) is administered subcutaneously. It is indicated for:

- Patients who have experienced a first clinical episode and are determined to be at high risk of developing clinically definite multiple sclerosis
- Ambulatory patients (i.e. who can walk unaided) with relapsing, remitting multiple sclerosis characterised by at least 2 attacks of neurological dysfunction over the preceding 2-year period

Interventions	<ul style="list-style-type: none"> • Interferon beta 1a • Peginterferon beta 1a • Interferon beta 1b • Glatiramer acetate
Population	People with multiple sclerosis (including people with clinically isolated syndrome, that is, a single demyelinating event, who are considered at high risk of developing multiple sclerosis)
Comparators	<ul style="list-style-type: none"> • Best supportive care without disease modifying treatment • If appropriate, the beta interferons and glatiramer acetate will be compared with each other
Outcomes	<ul style="list-style-type: none"> • relapse rate • severity of relapse • disability (for example, expanded disability status scale [EDSS]) • symptoms of multiple sclerosis such as fatigue, cognition and visual disturbance • freedom from disease activity • mortality • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The economic model will be based on the model used in the risk sharing scheme, including any changes that have been made to the model since 2002. The model parameters and inputs will be updated where necessary to reflect current costs, the NICE reference case and current practice, and any new data from the risk sharing scheme.</p> <p>If appropriate, any continuing contributions made by the companies who manufacturer technologies for multiple sclerosis to the infrastructure for multiple sclerosis management, should be taken into account in determining cost effectiveness.</p>
<p>Other considerations</p>	<p>It is recognised that best supportive care without a disease modifying treatment is not current established clinical practice for treating relapsing remitting multiple sclerosis. Best supportive care was the comparator for beta interferon and glatiramer acetate in TA32 and therefore is included as the comparator for this appraisal.</p> <p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Dimethyl fumarate for treating relapsing-remitting multiple sclerosis’ (2014). NICE Technology Appraisal 320. Review date to be confirmed</p> <p>‘Alemtuzumab for treating relapsing remitting multiple sclerosis’ (2014). NICE Technology Appraisal 312. Review date to be confirmed</p> <p>‘Teriflunomide for treating relapsing-remitting multiple sclerosis’ (2014). NICE Technology Appraisal 303.</p>

	<p>Review date to be confirmed</p> <p>'Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis (2012). NICE Technology Appraisal 254. Review date to be confirmed</p> <p>'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis' (2007). NICE Technology Appraisal 127. Review date to be confirmed</p> <p>'Beta interferon and glatiramer acetate for the treatment of multiple sclerosis' (2002) NICE Technology Appraisal 32.</p> <p>Related Guidelines:</p> <p>'Multiple sclerosis' (2014). NICE guideline 186 Review date December 2016.</p> <p>Related NICE Pathways:</p> <p>Multiple Sclerosis. NICE pathway http://pathways.nice.org.uk/</p>
<p>Related National Policy</p>	<p>NHS England. Manual for prescribed specialised services for 2013/14 chapter 11 adult specialist neurosciences services. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</p> <p>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1-5 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf</p>

Questions for consultation

The risk sharing scheme did not collect data from people with clinically isolated syndrome. Should people with clinically isolated syndrome be considered in this appraisal or be considered in a separate appraisal?

- Would all people with clinically isolated syndrome be expected to develop MS?
- Which technologies are used to treat clinically isolated syndrome?

Are there any other subgroups of people in whom beta interferon or glatiramer acetate are expected to be more clinically effective and cost effective or other groups that should be examined separately?

Should those drugs that were not part of technology appraisal 32, or part of the Risk Sharing Scheme (Plegridy and Extavia), but are beta interferons be included in this appraisal?

Are the outcomes listed appropriate?

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 proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient populations for which beta interferon and glatiramer acetate are 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 technologies;
- could 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.

Do you consider beta interferon or glatiramer acetate to be innovative in their potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of beta interferon or glatiramer acetate can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.