NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ozanimod for treating relapsing multiple sclerosis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ozanimod within its marketing authorisation for treating relapsing multiple sclerosis.

Background

Multiple sclerosis is a chronic, neurodegenerative disorder which affects the brain, optic nerves and spinal cord. It often results in progressive neurological impairment and severe disability. Multiple sclerosis 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.

Approximately 90,000 people in England have multiple sclerosis, and about 4,200 people are diagnosed each year.[1] The relapsing form of multiple sclerosis affects approximately 80–90% of people at the time of diagnosis.[2-5] It is characterised by periods of remission (when symptoms are mild or disappear altogether) followed by relapses (which may or may not result in residual disability). Relapsing-remitting multiple sclerosis can progress to secondary progressive multiple sclerosis. This is characterised by more persistent or gradually increasing disability; some patients with secondary progressive disease continue to have relapses.

Current pharmacological management of multiple sclerosis includes disease-modifying agents to reduce the frequency and severity of relapses and the rate of disease progression. These agents include beta interferon and glatiramer acetate which are not currently recommended by NICE (technology appraisal guidance 32, currently being reviewed), but were available in the NHS through a risk-sharing scheme; this scheme has now ended and a clinical commissioning policy is in place. NICE recommends the following treatment options:

- teriflunomide and dimethyl fumarate for active relapsing‑remitting multiple sclerosis, only if people do not have highly active or rapidly evolving severe relapsing‑remitting multiple sclerosis (technology appraisal guidance 303 and 320 respectively)

- alemtuzumab for active relapsing–remitting multiple sclerosis (technology appraisal guidance 312)

- fingolimod for highly active relapsing-remitting multiple sclerosis in adults who have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon (technology appraisal guidance 254)

- cladribine tablets for rapidly evolving severe relapsing–remitting multiple sclerosis or relapsing–remitting multiple sclerosis that has responded inadequately to treatment with disease-modifying therapy (technology appraisal guidance 493)

- natalizumab for rapidly-evolving severe relapsing-remitting multiple sclerosis (technology appraisal guidance 127)

- daclizumab for active relapsing–remitting multiple sclerosis (including highly active disease) or rapidly evolving severe relapsing-remitting multiple sclerosis, both previously treated with at least 2 disease-modifying therapies, and cannot be treated with any other disease-modifying therapies (technology appraisal guidance 441).

The technology

Ozanimod (brand name unknown, Celgene) is a sphingosine 1-phosphate 1 (S1PR1) and 5 (S1PR5) receptor modulator. Ozanimod inhibits inflammation by decreasing the number of circulating B and T lymphocytes. It may have the potential to prevent neurological damage by activating specific cells in the central nervous system. It is administered orally.

Ozanimod does not currently have a marketing authorisation in the UK for treating multiple sclerosis. It has been studied in clinical trials compared to interferon beta-1a and placebo in adults with relapsing multiple sclerosis.

Intervention	Ozanimod
Population	Adults with relapsing forms of multiple sclerosis
Comparators	For people with relapsing-remitting multiple sclerosis: • alemtuzumab • beta-interferon • cladribine tablets (only if the disease has responded inadequately to treatment with disease-modifying therapy, defined as 1 relapse in the previous year and MRI evidence of disease activity)

	• daclizumab (only if the disease has been previously treated with at least 2 disease-modifying therapies, and other disease-modifying therapies are contraindicated or otherwise unsuitable) • dimethyl fumarate • glatiramer acetate • teriflunomide • ocrelizumab (subject to ongoing NICE appraisal) For people with rapidly-evolving severe relapsing-remitting multiple sclerosis • alemtuzumab • cladribine tablets • daclizumab (only if the disease has been previously treated with at least 2 disease-modifying therapies, and other disease-modifying therapies are contraindicated or otherwise unsuitable) • natalizumab • ocrelizumab (subject to ongoing NICE appraisal) For people with highly active relapsing-remitting multiple sclerosis despite previous treatment • alemtuzumab • daclizumab (only if the disease has been previously treated with at least 2 disease-modifying therapies, and other disease-modifying therapies are contraindicated or otherwise unsuitable) • fingolimod • ocrelizumab (subject to ongoing NICE appraisal) For people with secondary progressive multiple sclerosis with active disease, evidenced by relapses • best supportive care

Outcomes	The outcome measures to be considered include: • 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.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account. For the comparators, the availability and cost of biosimilars should be taken into account.

Other considerations	If the evidence allows, the following subgroups will be considered: • people with relapsing-remitting multiple sclerosis • people with rapidly-evolving severe relapsing-remitting multiple sclerosis • people with highly active relapsing-remitting multiple sclerosis despite previous treatment • people with secondary progressive multiple sclerosis with active disease, evidenced by relapses. 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.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Cladribine for the treatment of relapsing-remitting multiple sclerosis (2017). NICE technology appraisal guidance 493. Review date December 2020. Daclizumab for treating relapsing–remitting multiple sclerosis (2017). NICE technology appraisal guidance 441. Review date April 2020. Dimethyl fumarate for treating relapsing-remitting multiple sclerosis (2014). NICE technology appraisal guidance 320. Review date to be confirmed. Alemtuzumab for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 312. Review date to be confirmed. Teriflunomide for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 303. Review date to be confirmed. Fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis (2012). NICE technology appraisal guidance 254. Review date to be confirmed. Natalizumab for the treatment of adults with highly active relapsing–remitting multiple sclerosis (2007). NICE technology appraisal guidance 127. Review date to be confirmed. Beta interferon and glatiramer acetate for the treatment of multiple sclerosis (2002). NICE technology appraisal

	guidance 32. Review ongoing, publication date to be confirmed. **Appraisals in development (including suspended appraisals):** Ocrelizumab for treating relapsing multiple sclerosis. NICE technology appraisal guidance [ID937]. Publication expected July 2018. Multiple sclerosis - interferon beta, glatiramer acetate (review TA32). NICE technology appraisal guidance [ID809]. Publication expected May 2018. Laquinimod for treating relapsing-remitting multiple sclerosis. NICE technology appraisals guidance [ID560] (suspended). **Related Guidelines:** Multiple sclerosis in adults (2014). NICE guideline 186. Review date to be confirmed. **Related Interventional Procedures:** Percutaneous venoplasty for chronic cerebrospinal venous insufficiency for multiple sclerosis (2012). NICE interventional procedure guidance 420. **Related Quality Standards:** Multiple sclerosis (2016) NICE quality standard QS108. **Related NICE Pathways:** Multiple sclerosis (2014) NICE pathway.
Related National Policy	Department of Health (2016) NHS outcomes framework 2016 to 2017: Domains 1–5. NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Chapter 11. Adult specialist neurosciences services NHS England (2014) Disease Modifying Therapies for Patients with multiple sclerosis (MS). Clinical commissioning policy reference D04/P/b.

Questions for consultation

Is ozanimod expected to be used to treat:

- secondary progressive multiple sclerosis with active disease, evidenced by relapses?
- rapidly-evolving severe relapsing-remitting multiple sclerosis?

- highly active relapsing-remitting multiple sclerosis despite previous treatment?

Have all relevant comparators for ozanimod been included in the scope? Which treatments are considered to be established clinical practice in the NHS for:

- relapsing-remitting multiple sclerosis?
- secondary progressive multiple sclerosis with active disease, evidenced by relapses?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom ozanimod is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider ozanimod for relapsing forms of multiple sclerosis will fit into the existing NICE pathway, Multiple sclerosis?

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 population for which ozanimod 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;
- 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 ozanimod to be innovative in its 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 ozanimod 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Multiple Sclerosis Society (2016) MS in the UK [accessed January 2018].

2. Multiple Sclerosis Society (2016) Types of MS [accessed January 2018].

3. NHS Choices (2016) Multiple sclerosis – overview [accessed January 2018].

4. Patient.info (2015) Multiple sclerosis [accessed January 2018].

5. MS International Federation (2016) Types of MS [accessed January 2018].