NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ocrelizumab for treating relapsing multiple sclerosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ocrelizumab within its marketing authorisation for treating relapsing forms of 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 85–90% of people at the time of diagnosis.[2,3] 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).

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)

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

- daclizumab for active relapsing–remitting multiple sclerosis (including highly active disease) previously treated with disease-modifying therapy, and for rapidly evolving severe relapsing–remitting multiple sclerosis, only if alemtuzumab is contraindicated or otherwise unsuitable (technology appraisal guidance 441).

The technology

Ocrelizumab (Ocrevus, Roche) is a monoclonal antibody that selectively targets the CD20 surface antigen on B cells (a type of white blood cell). It promotes the destruction of B cells by the body's immune system. Ocrelizumab is administered by intravenous infusion.

Ocrelizumab does not currently have a marketing authorisation in the UK for treating multiple sclerosis. It has been studied in clinical trials, compared with interferon beta-1a, in people with relapsing multiple sclerosis.

Intervention(s)	Ocrelizumab
Population(s)	People with relapsing forms of multiple sclerosis

Comparators	For people with relapsing-remitting multiple sclerosis: • alemtuzumab • dimethyl fumarate • teriflunomide • beta-interferon • glatiramer acetate • daclizumab (only if the disease has been previously treated with disease-modifying therapy, and alemtuzumab is contraindicated or otherwise unsuitable) For people with rapidly-evolving severe relapsing-remitting multiple sclerosis • alemtuzumab • natalizumab • daclizumab (only if alemtuzumab is contraindicated or otherwise unsuitable) For people with highly active relapsing-remitting multiple sclerosis despite previous treatment • alemtuzumab • fingolimod • daclizumab (only if alemtuzumab is contraindicated or otherwise unsuitable) 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. 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.

Other considerations	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. If the evidence allows, the following subgroups of people will be considered: • people whose disease has responded inadequately to previous treatment • people who could not tolerate previous treatment • 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 in whom alemtuzumab is contraindicated or otherwise unsuitable • people with secondary progressive multiple sclerosis with active disease, evidenced by relapses.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** 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)** Cladribine for the treatment of relapsing-remitting multiple sclerosis. NICE technology appraisal guidance [ID64]. Publication expected December 2017. Multiple sclerosis - interferon beta, glatiramer acetate (review TA32). NICE technology appraisal guidance [ID809]. Publication date to be confirmed. 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 (2016) Manual for Prescribed Specialised Services 2016/17. 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.

References

1. Multiple Sclerosis Society (2016) MS in the UK [accessed September 2017].

2. Multiple Sclerosis Society (2016) Types of MS [accessed September 2017].

3. MS International Federation (2016) Types of MS [accessed September 2017].