NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ocrelizumab for treating relapsing multiple sclerosis

Draft scope (pre-referral)

Draft 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 89,000 people in England have multiple sclerosis, and about 4,000 people are diagnosed each year[1]. The relapsing-remitting form of multiple sclerosis affects approximately 85–90%[2-4] of people at the time of diagnosis. 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), but are available in the NHS through a risk-sharing scheme. NICE has recommended dimethyl fumerate, alemtuzumab and teriflunomide as treatment options for relapsing-remitting multiple sclerosis (technology appraisal guidance 320,312 and 303 respectively). For people with rapidly-evolving severe relapsing-remitting multiple sclerosis, natalizumab is recommended as a treatment option (NICE technology appraisal guidance 127). NICE has recommended fingolimod as an option for treating 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 (NICE technology appraisal guidance 254).

The technology

Ocrelizumab (brand name unknown, 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 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 who have not had treatment previously • alemtuzumab • dimethyl fumarate • teriflunomide • beta-interferon • glatiramer acetate For people who have had previous treatment • alemtuzumab • dimethyl fumarate • teriflunomide For people with rapidly-evolving severe relapsing-remitting multiple sclerosis • alemtuzumab • natalizumab For people with highly active relapsing-remitting multiple sclerosis despite previous treatment • alemtuzumab • fingolimod

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 with relapsing-remitting multiple sclerosis whose disease has inadequately responded to previous treatment • people with relapsing-remitting multiple sclerosis who could not tolerate previous treatment.
Related NICE recommendations and NICE	**Related Technology Appraisals:** Dimethyl fumarate for treating relapsing-remitting multiple sclerosis (2014). NICE technology appraisal

Pathways	guidance 320. Review date April 2017. Alemtuzumab for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 312. Review date April 2017. Teriflunomide for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 303. Review date April 2017. Fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis (2012) NICE technology appraisal guidance 254. Date for review of guidance to be confirmed. Natalizumab for the treatment of adults with highly active relapsing–remitting multiple sclerosis (2007). NICE technology appraisal guidance 127. Date for review of guidance to be confirmed. Beta interferon and glatiramer acetate for the treatment of multiple sclerosis (2002). NICE technology appraisal guidance 32. Review ongoing, publication expected April 2017. **Terminated appraisals** Sativex as an add-on treatment of moderate to severe spasticity in multiple sclerosis (2002). NICE technology appraisal (terminated appraisal). **Appraisals in development (including suspended appraisals)** Multiple sclerosis - interferon beta, glatiramer acetate (review TA32) [ID809]. NICE technology appraisal. Publication expected: April 2017. Multiple sclerosis (primary-progressive) - fingolimod [ID62]. NICE technology appraisal (suspended). Laquinimod for treating relapsing-remitting multiple sclerosis [ID560]. NICE technology appraisal (suspended). Cladribine for the treatment of relapsing-remitting multiple sclerosis [ID64]. NICE technology appraisal (suspended). **Proposed technology appraisals** Biotin for primary and secondary progressive multiple sclerosis. Proposed NICE technology appraisal [ID919]. Publication date to be confirmed. **Related Guidelines:** Multiple sclerosis (2014). NICE guideline 186. Review

	date December 2016. **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	**NHS England** NHS England (January 2014) Manual for prescribed specialised services 2013/2014, chapter 11 (page 41): Adult specialist neurosciences services NHS England (May 2014) Disease Modifying Therapies for Patients with multiple sclerosis (MS). Clinical commissioning policy reference D04/P/b. **Department of Health** Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1–5.

Questions for consultation

Is ocrelizumab expected to be used to treat:

- secondary progressive multiple sclerosis with active disease, evidenced by relapses?
- clinically isolated syndrome, that is, a single demyelinating event, who are considered at high risk of developing multiple sclerosis?
- rapidly-evolving severe relapsing-remitting multiple sclerosis?
- highly active relapsing-remitting multiple sclerosis despite previous treatment?

Have all relevant comparators for ocrelizumab 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?

- clinically isolated syndrome, that is, a single demyelinating event, who are considered at high risk of developing multiple sclerosis?

Are the outcomes listed appropriate?

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

Where do you consider ocrelizumab will fit into the existing NICE pathway for 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 ocrelizumab 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 ocrelizumab 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 ocrelizumab 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.

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)

References

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

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

3 Murray T (2006) Diagnosis and treatment of multiple sclerosis. British Medical Journal 332: 525–7

4 Scolding N, Barnes D, Cader S et al. (2015). Association of British Neurologists: revised (2015) guidelines for prescribing disease-modifying treatments in multiple sclerosis Practical Neurology 0: 1–7