NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ocrelizumab for treating primary progressive 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 primary progressive 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]. Most people have relapsing-remitting multiple sclerosis, which 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). Approximately 10%[2-4] of people are diagnosed with primary progressive multiple sclerosis, in which symptoms develop and worsen over time without periods of remission.

There are currently no licensed treatments that slow down or stop disease progression in primary progressive multiple sclerosis. NICE clinical guideline 186 recommends ways to manage the symptoms of multiple sclerosis, including pharmacological treatments, physiotherapy and exercise programmes, occupational therapy, cognitive behavioural therapy, fatigue management, and speech therapy.

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 treating multiple sclerosis. It has been studied in clinical trials, compared with placebo, in people with primary progressive multiple sclerosis.

Intervention(s)	Ocrelizumab

Population(s)	People with primary progressive multiple sclerosis
Comparators	Established clinical management without ocrelizumab
Outcomes	The outcome measures to be considered include: • disability (for example, expanded disability status scale [EDSS] or time to walk 25 feet) • symptoms of multiple sclerosis such as fatigue, cognition and visual disturbance • relapse rate • severity of relapse • 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.
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.
Related NICE recommendations and NICE Pathways	**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 (primary-progressive) - fingolimod [ID62]. NICE technology appraisal (suspended).

	Proposed technical appraisals Biotin for the first line treatment of primary or 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

Have all relevant comparators for ocrelizumab been included in the scope?

What interventions are included in established clinical management for primary progressive multiple sclerosis?

Are the outcomes listed appropriate?

Are there any 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