NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ofatumumab for treating relapsing multiple sclerosis

Draft scope (pre-referral)

Draft remit/appraisal objective

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

Background

Multiple sclerosis is a chronic, neurological condition 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 which varies in severity and rate of 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. Relapsing-remitting multiple sclerosis is the most common clinical form of multiple sclerosis. It is characterised by periods of remission (when symptoms can be mild and are generally stable 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 people with secondary progressive disease continue to have relapses.

Approximately 100,000 people in the UK have multiple sclerosis, and about 5,000 people are diagnosed each year.[1] Approximately 85% of people are diagnosed with relapsing–remitting multiple sclerosis and around 50% of people transition to secondary progressive multiple sclerosis within 20 years.[2] A small number of people are diagnosed with secondary progressive multiple sclerosis without a previous diagnosis of relapsing–remitting multiple sclerosis.

Current pharmacological management of relapsing–remitting multiple sclerosis includes disease-modifying agents to reduce the frequency and severity of relapses and the rate of disease progression.

NICE recommends the following treatment options for relapsing–remitting multiple sclerosis:

- ocrelizumab for active relapsing–remitting multiple sclerosis only if alemtuzumab is contraindicated or otherwise unsuitable (NICE TA533)

- interferon beta-1a and glatiramer acetate for relapsing–remitting multiple sclerosis and interferon beta-1b for relapsing–remitting multiple sclerosis with 2 or more relapses within the last 2 years (NICE TA527)

- 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 (NICE TA303 and TA320 respectively)

- alemtuzumab for active relapsing–remitting multiple sclerosis (NICE TA312) [1]

- 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 (NICE TA254)

- natalizumab for rapidly evolving severe relapsing–remitting multiple sclerosis (NICE TA127)

- cladribine tablets for treating highly active multiple sclerosis only for rapidly evolving severe relapsing–remitting disease or disease that has responded inadequately to treatment with disease-modifying therapy (NICE TA493).

Treatments for relapsing–remitting multiple sclerosis are also used for people with active secondary progressive multiple sclerosis, as evidenced by relapses. NICE TA527 recommends interferon beta-1b for treating secondary progressive multiple sclerosis in people with continuing relapses.

The technology

Ofatumumab (brand name unknown, Novartis) 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. Ofatumumab is administered by subcutaneous injection.

Ofatumumab does not currently have a marketing authorisation in the UK for treating multiple sclerosis. It has been studied in clinical trials, compared with teriflunomide in people with relapsing multiple sclerosis.

Intervention(s)	Ofatumumab
Population(s)	People with relapsing multiple sclerosis
Comparators	For people with relapsing–remitting multiple sclerosis: • beta interferon • dimethyl fumarate • glatiramer acetate • teriflunomide • ocrelizumab • peginterferon beta-1a • ozanimod (subject to ongoing NICE appraisal) For people with highly active relapsing–remitting multiple

[1] In October 2019, the European Medicines Agency's pharmacovigilance risk assessment committee recommended restricting alemtuzumab to use in adults with relapsing remitting multiple sclerosis that is highly active despite adequate treatment with at least one disease-modifying therapy or if the disease is worsening rapidly with at least two disabling relapses in a year and brain-imaging showing new damage. The recommendations in NICE TA312 will be updated to reflect this in due course.

	sclerosis despite previous treatment: • alemtuzumab[1] • cladribine • fingolimod • ocrelizumab (only if alemtuzumab[1] is contraindicated or otherwise unsuitable) • ozanimod (subject to ongoing NICE appraisal) For people with rapidly-evolving severe relapsing–remitting multiple sclerosis: • alemtuzumab[1] • cladribine • natalizumab • ocrelizumab (only if alemtuzumab[1] is contraindicated or otherwise unsuitable) • ozanimod (subject to ongoing NICE appraisal) For people with active secondary progressive multiple sclerosis (evidenced by continuing relapses): • established clinical management, including interferon beta-1b or other disease modifying therapies used outside their marketing authorisations • siponimod (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • relapse rate • severity of relapse • disability (for example, expanded disability status scale [EDSS]) • disease progression • symptoms of multiple sclerosis (such as fatigue, cognition and visual disturbance) • freedom from disease activity (for example lesions on MRI scans) • 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 commercial arrangements for the intervention, comparator and subsequent treatment 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 subgroup of people will be considered:
	• people who could not tolerate previous treatment
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:**
	Ocrelizumab for treating relapsing–remitting multiple sclerosis (2018). NICE technology appraisal guidance 533. Review date July 2021.
	Beta interferons and glatiramer acetate for treating multiple sclerosis (2018). NICE technology appraisal guidance 527. Review date June 2021.
	Cladribine tablets for treating relapsing–remitting multiple sclerosis (2017). NICE technology appraisal guidance 493. Review date December 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.
	Appraisals in development (including suspended appraisals)
	[Ozanimod for treating relapsing multiple sclerosis](#). NICE technology appraisals guidance [ID1294]. Expected publication date July 2020.
	[Peginterferon beta-1a for treating relapsing–remitting multiple sclerosis](#) [ID1521].Expected publication date to be confirmed.
	[Siponimod for treating secondary progressive multiple sclerosis](#) [ID1304]. Expected publication date June 2020.
	Related Guidelines:
	[Multiple sclerosis in adults](#) (2014). NICE guideline 186. Update 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	The NHS Long Term Plan, 2019. [NHS Long Term Plan](#)
	NHS England (2018/2019) Section 105. NHS manual for prescribed specialist services (2018/2019)
	https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf
	NHS England (May 2014) Clinical commissioning policy: [Disease Modifying Therapies for Patients with multiple sclerosis (MS)](#).
	Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1-4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Is ofatumumab likely to be used in patients with active secondary progressive multiple sclerosis (evidenced by continuing relapses)?

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

Which treatments are considered to be established clinical practice in the NHS for relapsing–remitting multiple sclerosis and secondary progressive multiple sclerosis?

Are the outcomes listed appropriate?

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

Where do you consider ofatumumab will fit into the existing NICE pathway, Multiple sclerosis (2014)?

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 ofatumumab 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 ofatumumab 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 ofatumumab 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).

References

1. Multiple Sclerosis Society (2018) MS in the UK [accessed September 2019].

2. Multiple Sclerosis Trust (2017) Secondary progressive multiple sclerosis. Accessed September 2019