

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Ofatumumab for treating relapsing multiple sclerosis

Final scope

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 (where people may have no symptoms, or they may be relatively stable) 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 130,000 people in the UK have multiple sclerosis, and about 7,000 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 TA616](#)).
- peginterferon beta-1a for treating relapsing–remitting multiple sclerosis ([NICE TA624](#))

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 active relapsing–remitting multiple sclerosis: <ul style="list-style-type: none"> • beta interferon • dimethyl fumarate • glatiramer acetate • teriflunomide • ocrelizumab • peginterferon beta-1a

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.

	<ul style="list-style-type: none"> • ozanimod (subject to ongoing NICE appraisal) <p>For people with highly active relapsing–remitting multiple sclerosis despite previous treatment:</p> <ul style="list-style-type: none"> • alemtuzumab¹ • cladribine • fingolimod • ocrelizumab (only if alemtuzumab¹ is contraindicated or otherwise unsuitable) • ozanimod (subject to ongoing NICE appraisal) <p>For people with rapidly-evolving severe relapsing–remitting multiple sclerosis:</p> <ul style="list-style-type: none"> • alemtuzumab¹ • cladribine • natalizumab • ocrelizumab (only if alemtuzumab¹ is contraindicated or otherwise unsuitable) • ozanimod (subject to ongoing NICE appraisal) <p>For people with active secondary progressive multiple sclerosis (evidenced by continuing relapses):</p> <ul style="list-style-type: none"> • established clinical management, including interferon beta-1b or other disease modifying therapies used outside their marketing authorisations • siponimod (subject to ongoing NICE appraisal)
<p>Outcomes</p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • 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.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
<p>Other considerations</p>	<p>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.</p> <p>If the evidence allows, the following subgroup of people will be considered:</p> <ul style="list-style-type: none"> • people who could not tolerate previous treatment
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>Peginterferon beta-1a for treating relapsing–remitting multiple sclerosis (2020). NICE technology appraisal guidance 624. Review date 2023</p> <p>Cladribine for treating relapsing–remitting multiple sclerosis (2019). NICE technology appraisal guidance 616. Review date 2022.</p> <p>Ocrelizumab for treating relapsing–remitting multiple sclerosis (2018). NICE technology appraisal guidance 533. Review date July 2021.</p> <p>Beta interferons and glatiramer acetate for treating multiple sclerosis (2018). NICE technology appraisal guidance 527. Review date June 2021.</p> <p>Dimethyl fumarate for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 320. Review date to be confirmed.</p> <p>Alemtuzumab for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 312. Review date to be confirmed.</p> <p>Teriflunomide for treating relapsing–remitting multiple</p>

	<p>sclerosis (2014). NICE technology appraisal guidance 303. Review date to be confirmed.</p> <p>Fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis (2012). NICE technology appraisal guidance 254. Review date to be confirmed.</p> <p>Natalizumab for the treatment of adults with highly active relapsing–remitting multiple sclerosis (2007). NICE technology appraisal guidance 127. Review date to be confirmed.</p> <p>Appraisals in development (including suspended appraisals)</p> <p>Ozanimod for treating relapsing multiple sclerosis. NICE technology appraisals guidance [ID1294]. Expected publication date TBC.</p> <p>Siponimod for treating secondary progressive multiple sclerosis [ID1304]. Expected publication date TBC.</p> <p>Related Guidelines:</p> <p>Multiple sclerosis in adults (2014, updated 2019). NICE guideline 186..</p> <p>Related Interventional Procedures:</p> <p>Percutaneous venoplasty for chronic cerebrospinal venous insufficiency for multiple sclerosis (2019). NICE interventional procedure guidance 640.</p> <p>Related Quality Standards:</p> <p>Multiple sclerosis (2016) NICE quality standard QS108.</p> <p>Related NICE Pathways:</p> <p>Multiple sclerosis (2014) NICE pathway.</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) Section 105. NHS manual for prescribed specialist services (2018/2019)</p> <p>https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf</p> <p>NHS England (May 2014) Clinical commissioning policy: Disease Modifying Therapies for Patients with multiple sclerosis (MS).</p> <p>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</p>

References

1. Multiple Sclerosis Society (2020) [MS in the UK](#). Accessed May 2020.

2. Multiple Sclerosis Trust (2017) [Secondary progressive multiple sclerosis](#).
Accessed May 2020.