NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Natalizumab for treating highly active relapsing-remitting multiple sclerosis

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of natalizumab within its marketing authorisation for treating highly active relapsing-remitting 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, which is characterised by more persistent or gradually increasing disability; some people with secondary progressive disease continue to have relapses.

Approximately 105,800 people in England have multiple sclerosis, and about 4,950 people are diagnosed each year.[1] Over 80% of people are diagnosed with relapsing–remitting multiple sclerosis and around 50% of those people transition to secondary progressive multiple sclerosis within 15 to 20 years of diagnosis.[2] A small number of people (over 1 in 10) are diagnosed with primary progressive multiple sclerosis without a previous diagnosis of relapsing–remitting multiple sclerosis.[2]

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 already recommends natalizumab as a first line treatment option for people with rapidly evolving severe relapsing–remitting multiple sclerosis (NICE TA127). NICE recommends the following treatment options for previously treated relapsing–remitting multiple sclerosis:

- ocrelizumab for active relapsing–remitting multiple sclerosis only if alemtuzumab is contraindicated or otherwise unsuitable (NICE TA533)
- alemtuzumab for highly active relapsing–remitting multiple sclerosis despite a full and adequate course of treatment with at least 1 disease-modifying therapy (NICE TA312)
- 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)

- cladribine tablets for treating highly active multiple sclerosis only if the person has rapidly evolving severe relapsing–remitting disease or disease that has responded inadequately to treatment with disease-modifying therapy (NICE TA616).

The technology

Natalizumab (Tysabri, Biogen) has been licensed as single disease modifying therapy in adults with highly active relapsing remitting multiple sclerosis for the following people:

- People with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy

OR

- People with rapidly evolving severe RRMS defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain Magnetic Resonance Imaging (MRI) or a significant increase in T2 lesion load as compared to a previous recent MRI.

NICE TA127 guidance for natalizumab covers the second part of the population above. Since the guidance was published, a marketing authorisation extension has been granted for "people with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy".

Intervention(s)	Natalizumab
Population(s)	Adults with highly active relapsing remitting multiple sclerosis despite a full and adequate course of treatment with at least one disease modifying therapy The population will exclude those already covered in NICE TA127.

Subgroups	If the evidence allows, the following subgroups of patients will be considered: • patients with relapsing–remitting multiple sclerosis whose disease has inadequately responded to treatment with disease-modifying therapy • patients with relapsing–remitting multiple sclerosis whose disease is intolerant to treatment with disease-modifying therapy • patients with highly active relapsing–remitting multiple sclerosis • patients with rapidly evolving severe relapsing–remitting multiple sclerosis.
Comparators	For people with highly active relapsing–remitting multiple sclerosis despite previous treatment: • alemtuzumab • cladribine • fingolimod • ocrelizumab (only if alemtuzumab is contraindicated or otherwise unsuitable).
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 of 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. 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 considered.
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	**Related Technology Appraisals:** Cladribine tablets for treating relapsing–remitting multiple sclerosis (2017). NICE technology appraisal guidance 616. Review date 2022. Ocrelizumab for treating relapsing–remitting multiple sclerosis (2018). NICE technology appraisal guidance 533. Review date July 2021. Alemtuzumab for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 312. 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. **Related appraisals in development:** Diroximel fumarate for treating relapsing-remitting multiple sclerosis. NICE technology appraisals guidance [ID1673]. Expected publication date May 2022.

	Related Guidelines: Multiple sclerosis in adults: management (2019). NICE guideline 186. **Guidelines in development:** Multiple sclerosis in adults: management. Publication expected June 2022. **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 National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 11. Adult specialist neurosciences services. NHS England (2019) Treatment Algorithm for Multiple Sclerosis: Disease-Modifying Therapies

Questions for consultation

Where do you consider natalizumab will fit into the existing care pathway for highly active relapsing-remitting multiple sclerosis?

Is there an overlap in the population of the marketing authorisation (MA) and the MA extension (that is, between NICE TA127 and the population in this scope)? **Original MA** indication: Patients with rapidly evolving severe RRMS defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain Magnetic Resonance Imaging (MRI) or a significant increase in T2 lesion load as compared to a previous recent MRI. **MA extension indication**: Patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy (DMT)

Would natalizumab be a candidate for managed access?

Do you consider natalizumab 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 natalizumab can result in any potential 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 committee to take account of these benefits.

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 natalizumab is 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost-comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Public Health England (2020) Multiple sclerosis: prevalence, incidence and smoking status - data briefing. Accessed March 2022.

2. National Health Service (2022) Multiple Sclerosis. Accessed March 2022.