NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Natalizumab and Tyruko (natalizumab biosimilar) for treating highly active relapsing-remitting multiple sclerosis after at least one disease modifying therapy [ID6369]

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of natalizumab (Tysabri) and Tyruko (natalizumab biosimilar) within its marketing authorisation for treating highly active relapsing-remitting multiple sclerosis after at least one disease modifying therapy.

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.

Over 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,[2] and around 50% of people transition to secondary progressive multiple sclerosis within 20 years.[3] 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 previously treated highly active relapsing–remitting multiple sclerosis:

- ponesimod and ofatumumab for active relapsing–remitting multiple sclerosis (NICE TA706)
- 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).

- ocrelizumab and ofatumumab for active relapsing–remitting multiple sclerosis only if alemtuzumab is contraindicated or otherwise unsuitable (NICE TA533 and NICE TA706)

- 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)

The technology

Natalizumab (Tysabri, Biogen) and natalizumab biosimilar (Tyruko, Sandoz) have been licensed as single disease modifying therapy in adults with highly active relapsing remitting multiple sclerosis for the following people:

- 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.

OR

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

NICE already recommends natalizumab as a first-line treatment option for people with rapidly evolving severe relapsing–remitting multiple sclerosis (NICE TA127); covering the first part of the population above. This is why this scope focuses only on highly active relapsing-remitting multiple sclerosis after at least one disease modifying therapy. Natalizumab (Tysabri) has a marketing authorisation for subcutaneous and intravenous administration, whereas natalizumab biosimilar (Tyruko) has a licence for intravenous administration only.

Intervention(s)	• natalizumab (Tysabri) • natalizumab biosimilar (Tyruko)
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

Comparators	Standard care without natalizumab or natalizumab biosimilar, including but not limited to:
	• For people with disease activity after 1 disease modifying therapy (DMT):
	  ○ dimethyl fumarate
	  ○ diroximel fumarate
	  ○ glatiramer acetate
	  ○ interferon beta 1a
	  ○ interferon beta 1b
	  ○ teriflunomide
	• For people with disease activity after 2 DMTs:
	  ○ alemtuzumab
	  ○ cladribine (subject to NICE evaluation)
	  ○ fingolimod
	• For people with disease activity after 1 or 2 DMTs:
	  ○ ocrelizumab
	  ○ ofatumumab
	  ○ ponesimod

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 (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. 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. The availability and cost of biosimilar and generic products should 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.
Related NICE recommendations	**Related technology appraisals:** Diroximel fumarate for treating relapsing-remitting multiple sclerosis (2022). NICE technology appraisals guidance 794. Ponesimod for treating relapsing–remitting multiple sclerosis (2022). NICE technology appraisals guidance 767. Ozanimod for treating relapsing–remitting multiple sclerosis (2021). NICE technology appraisals guidance 706. Ofatumumab for treating relapsing multiple sclerosis (2021). NICE technology appraisals guidance 699. Cladribine tablets for treating relapsing–remitting multiple sclerosis (2017). NICE technology appraisal guidance 616. Ocrelizumab for treating relapsing–remitting multiple sclerosis (2018). NICE technology appraisal guidance 533. Alemtuzumab for treating relapsing–remitting multiple sclerosis (updated 2020). NICE technology appraisal guidance 312. Fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis (2012). NICE technology appraisal guidance 254. Natalizumab for the treatment of adults with highly active relapsing–remitting multiple sclerosis (2007). NICE technology appraisal guidance 127. **Technology appraisals in development:**

	Cladribine for treating relapsing multiple sclerosis. NICE technology appraisal [ID6263] **Related NICE guidelines:** Multiple sclerosis in adults: management (2022) NICE clinical guideline NG220. **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 (2023) NHS manual for prescribed specialist services (2023) Chapter 11. Adult specialist neurosciences services. NHS England (2019) Treatment Algorithm for Multiple Sclerosis: Disease-Modifying Therapies

Questions for consultation

What criteria would be used to define highly active relapsing remitting multiple sclerosis in clinical practice?

Where do you consider natalizumab and natalizumab biosimilar will fit into the existing care pathway for highly active relapsing remitting multiple sclerosis despite a full and adequate course of treatment with at least one disease modifying therapy?

Does the current scope match the NHS treatment algorithm appropriately?

How often are beta interferons used in untreated people with highly active relapsing remitting multiple sclerosis?

What disease modifying treatments, other than beta interferons, are used in untreated people with highly active relapsing remitting multiple sclerosis? Are these treatments associated with different outcomes to beta interferons?

Would ofatumumab and ponesimod be used in people with highly active relapsing remitting multiple sclerosis despite a full and adequate course of treatment after at least one disease modifying therapy?

Would subcutaneous and intravenous formulations of natalizumab be used interchangeably? If not, in whom would each formulation be used? Would the comparators be different for each formulation?

Would natalizumab and natalizumab biosimilar be a candidate for managed access?

Do you consider that the use of natalizumab and natalizumab biosimilar 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 the treatments are 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 appraise this technology through its Multiple Technology Appraisal (MTA) 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/process/pmg36/chapter/introduction-to-health-technology-evaluation).

- Are there any other technologies that it would be appropriate to include in an MTA with natalizumab and Tyruko (natalizumab biosimilar)?

References

1. Multiple Sclerosis Society (2020) MS in the UK report [accessed November 2023].

2. Multiple Sclerosis Society (2019) Relapsing remitting MS (RRMS) [accessed November 2023].

3. Barzegar M, Najdaghi S, Afshari-Safavi A et al (2021). Early predictors of conversion to secondary progressive multiple sclerosis. Multiple sclerosis and related disorders, 54, 103115.