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**

**Final scope**

# Final remit/evaluation objective

To appraise the clinical and cost effectiveness of natalizumab (Tysabri) and natalizumab biosimilar (Tyruko) 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 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 TA76](https://www.nice.org.uk/guidance/ta767)7 and [NICE TA699](https://www.nice.org.uk/guidance/ta699))
* 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](https://www.nice.org.uk/guidance/ta616)).
* ocrelizumab and ofatumumab for active relapsing–remitting multiple sclerosis only if alemtuzumab is contraindicated or otherwise unsuitable ([NICE TA533](https://www.nice.org.uk/guidance/ta533) and [NICE TA706](https://www.nice.org.uk/guidance/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](https://www.nice.org.uk/guidance/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](https://www.nice.org.uk/guidance/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](https://www.nice.org.uk/guidance/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.

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| **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):   + glatiramer acetate   + interferon beta 1a   + interferon beta 1b   + alemtuzumab   + cladribine tablets   + fingolimod   + ocrelizumab (if alemtuzumab contraindicated or otherwise unsuitable)   + ofatumumab   + ponesimod   + autologous haematopoietic stem cell transplantation |
| **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.  Natalizumab may increase the risk of developing progressive multifocal leukoencephalopathy caused by the JC virus. The economic modelling should include the costs associated with anti-JCV antibody testing in people with highly active relapsing-remitting multiple sclerosis who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the test. See section 4.8 of the unified manual (available here: <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).  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](https://www.nice.org.uk/guidance/indevelopment/gid-ta10714) (2022). NICE technology appraisals guidance 794.  [Ponesimod for treating relapsing–remitting multiple sclerosis](https://www.nice.org.uk/guidance/ta767) (2022). NICE technology appraisals guidance 767.  [Ozanimod for treating relapsing–remitting multiple sclerosis](https://www.nice.org.uk/guidance/ta706) (2021). NICE technology appraisals guidance 706.  [Ofatumumab for treating relapsing multiple sclerosis](https://www.nice.org.uk/guidance/ta699) (2021). NICE technology appraisals guidance 699.  [Cladribine tablets for treating relapsing–remitting multiple sclerosis](https://www.nice.org.uk/guidance/TA616) (2017). NICE technology appraisal guidance 616.  [Ocrelizumab for treating relapsing–remitting multiple sclerosis](https://www.nice.org.uk/guidance/TA533) (2018). NICE technology appraisal guidance 533.  [Alemtuzumab for treating relapsing–remitting multiple sclerosis](http://www.nice.org.uk/Guidance/TA312) (updated 2020). NICE technology appraisal guidance 312.  [Fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis](http://www.nice.org.uk/Guidance/TA254) (2012). NICE technology appraisal guidance 254.  [Natalizumab for the treatment of adults with highly active relapsing–remitting multiple sclerosis](http://www.nice.org.uk/Guidance/TA127) (2007). NICE technology appraisal guidance 127.  **Technology appraisals in development:**  [Cladribine for treating relapsing multiple sclerosis](https://www.nice.org.uk/guidance/indevelopment/gid-ta11293). NICE technology appraisal [ID6263]  **Related NICE guidelines:**  [Multiple sclerosis in adults: management](https://www.nice.org.uk/guidance/NG220) (2022) NICE clinical guideline NG220.  **Related interventional procedures:**  [Percutaneous venoplasty for chronic cerebrospinal venous insufficiency for multiple sclerosis](http://www.nice.org.uk/Guidance/IPG420) (2012). NICE interventional procedure guidance 420.  **Related quality standards:**  [Multiple sclerosis](https://www.nice.org.uk/guidance/qs108) (2016). NICE quality standard QS108. |
| **Related National Policy** | The NHS Long Term Plan, 2019. [NHS Long Term Plan](https://www.longtermplan.nhs.uk/publication/nhs-long-term-plan/)  NHS England (2023) [NHS manual for prescribed specialist services (2023)](https://www.england.nhs.uk/publication/manual-for-prescribed-specialised-services/) Chapter 11. Adult specialist neurosciences services.  NHS England (20239) [Treatment Algorithm for Multiple Sclerosis: Disease-Modifying Therapies](https://www.england.nhs.uk/wp-content/uploads/2018/09/ms-algorithm-v5.pdf) |

# References

1. Multiple Sclerosis Society (2020) [MS in the UK](https://www.mssociety.org.uk/care-and-support/resources-and-publications/publications-search/ms-in-the-uk) report [accessed November 2023].
2. Multiple Sclerosis Society (2019) [Relapsing remitting MS](https://www.mssociety.org.uk/about-ms/types-of-ms/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](https://www.msard-journal.com/article/S2211-0348(21)00382-5/fulltext). Multiple sclerosis and related disorders, 54, 103115.