NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Tolebrutinib for treating non-relapsing secondary progressive multiple sclerosis ID6351

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of tolebrutinib within its marketing authorisation for treating non-relapsing secondary progressive 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, sensory disturbance, limb weakness and gait impairment, spasticity, chronic fatigue, speech problems, incontinence, lack of coordination, visual failure, and cognitive impairment.

Most people present with relapsing–remitting multiple sclerosis. This 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). Most people with relapsing–remitting multiple sclerosis will develop secondary progressive disease. This is characterised by more persistent or gradually increasing disability. Active secondary progressive multiple sclerosis is characterised by inflammatory MRI activity or relapses. Non-relapsing secondary progressive multiple sclerosis includes:

- non-active secondary progressive multiple sclerosis,
- active secondary progressive multiple sclerosis where there is only MRI activity and no relapses.

Over 150,000 people in the UK have multiple sclerosis, and about 7,100 people are diagnosed each year.[1] Approximately 85% are diagnosed with relapsing–remitting multiple sclerosis.[2-3] Around 50% of people with relapsing–remitting multiple sclerosis transition to secondary progressive multiple sclerosis within 20 years and 93% progress within 30 years.[4] A small number of people are diagnosed with secondary progressive multiple sclerosis without a previous diagnosis of relapsing–remitting multiple sclerosis. It is unclear what proportion of people with secondary progressive multiple sclerosis have non-relapsing disease in the UK.

Current pharmacological management of multiple sclerosis includes disease-modifying agents to reduce the frequency and severity of relapses and the rate of disease progression. There are currently no disease-modifying therapies recommended for the whole non-relapsing secondary progressive multiple sclerosis population.

NICE recommends the following treatment options for active secondary progressive multiple sclerosis:

- Siponimod for treating secondary progressive multiple sclerosis with evidence of disease activity (NICE TA656)

- Interferon beta-1b (Extavia) for treating secondary progressive multiple sclerosis with continuing relapses (NICE TA527)

The technology

Tolebrutinib (brand name unknown, Sanofi) does not currently have a marketing authorisation in the UK for any indication. It has been studied in clinical trials compared with placebo in people with non-relapsing secondary progressive multiple sclerosis.

Intervention(s)	Tolebrutinib
Population(s)	Adults with non-relapsing secondary progressive multiple sclerosis
Subgroups	If the evidence allows the following subgroups will be considered: • People with non-active secondary progressive multiple sclerosis • People with active secondary progressive multiple sclerosis where there is only MRI activity and no relapses.
Comparators	Established clinical management without tolebrutinib, including but not limited to: • Siponimod (for people with active non-relapsing secondary progressive multiple sclerosis) • Best supportive care
Outcomes	The outcome measures to be considered include: • disability (for example, expanded disability status scale [EDSS]) • disability progression • symptoms of multiple sclerosis (such as fatigue, cognition or 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. 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 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:** Siponimod for treating secondary progressive multiple sclerosis (2020) NICE technology appraisal guidance TA656. Beta interferons and glatiramer acetate for treating multiple sclerosis (2018) NICE technology appraisal guidance TA527. **Related NICE guidelines:** Multiple sclerosis in adults: management (2022) NICE guideline NG220. **Related interventional procedures:** Percutaneous venoplasty for chronic cerebrospinal venous insufficiency in multiple sclerosis (2019) NICE interventional procedures guidance IPG640. **Related quality standards:** Multiple sclerosis (2016) NICE quality standard QS108.

References

1. Multiple Sclerosis Society MS in the UK [accessed May 2025]
2. Multiple Sclerosis Society Relapsing remitting MS (RRMS) [accessed March 2025]
3. MS International Federation (2022) Types of MS [accessed March 2025]
4. Barzegar M, Najdaghi S, Afshari-Safavi A et al (2021). Early predictors of conversion to secondary progressive multiple sclerosis. Mult Scler Relat Disord; 54. DOI: https://doi.org/10.1016/j.msard.2021.103115