

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Siponimod for treating secondary progressive multiple sclerosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of siponimod within its marketing authorisation for treating secondary progressive multiple sclerosis in adults.

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 (RRMS) is the most common clinical form of MS. It is characterised by periods of remission (when symptoms can be mild and are generally stable or disappear altogether) followed by relapses (which may or may not result in residual disability). Many people with RRMS will develop secondary progressive multiple sclerosis (SPMS), which is characterised by more persistent or gradually increasing disability commonly without relapses, however some people continue to experience relapses.

Approximately 100,000 people in the UK have MS, with 5,000 people diagnosed each year.¹ Approximately 85% of people are diagnosed with the RRMS form and 50% of people transition from RRMS to SPMS within 20 years.² A small number of people are diagnosed with SPMS without a previous diagnosis of RRMS. There are an estimated 38,000 people in the UK with SPMS.^{3,4}

Current pharmacological management of MS includes immune modulating disease-modifying therapies that aim to reduce the frequency and severity of relapses. They are therefore typically used before SPMS diagnosis, or for people with active SPMS, as evidenced by relapses. NICE technology appraisal guidance 527 recommends interferon beta-1b for treating SPMS in people with continuing relapses. Current clinical care also involves treatments to manage specific symptoms of MS, which may include high dose steroids.

The technology

Siponimod (Mayzent, Novartis) is a selective agonist of the sphingosine-1 phosphate (S1P) receptors 1 and 5. The drug selectively binds to circulating

lymphocytes which reversibly inhibits egress of lymphocytes from the lymph nodes, leading to a reduction in disease activity. It is administered orally.

Siponimod does not currently have a marketing authorisation in the UK for treating multiple sclerosis. It has been studied in clinical trials compared with placebo in people with SPMS.

Intervention	Siponimod
Population	People with secondary progressive multiple sclerosis
Comparators	<ul style="list-style-type: none"> • Established clinical management, including disease modifying therapies used outside their marketing authorisations <p>For people with active disease, evidenced by relapses:</p> <ul style="list-style-type: none"> • Interferon beta 1b
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • disability (for example, expanded disability status scale [EDSS]) • disease progression • relapse rate and severity (for those with active disease) • symptoms of multiple sclerosis such as fatigue, cognition and visual disturbance • MRI parameters (for example, lesion counts and brain volume change) • freedom from disease activity • mortality • adverse effects of treatment • health-related quality of life.

Economic analysis	<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>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>
Other considerations	<p>The availability and cost of biosimilar products should be taken into account.</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>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>‘Beta-interferons and glatiramer acetate for treating multiple sclerosis’ (2018). NICE Technology Appraisal 527. Review date June 2021.</p> <p>Appraisals in development (including suspended appraisals)</p> <p>‘Biotin for treating primary and secondary progressive multiple sclerosis’ NICE technology appraisals guidance [ID919]. Publication date to be confirmed (suspended appraisal)</p> <p>Related Guidelines:</p> <p>Multiple sclerosis in adults (2014). NICE guideline 186. Update proposed, date to be confirmed.</p> <p>Related Interventional Procedures:</p> <p>Percutaneous venoplasty for chronic cerebrospinal venous insufficiency in multiple sclerosis (2019). NICE interventional procedure guidance 640. Review date January 2019.</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 (2018) [MS in the UK](#) [accessed July 2019].
2. Multiple Sclerosis Trust (2017) [Secondary progressive multiple sclerosis](#). Accessed September 2018
3. Khurana V, Sharma H, Medin J (2018) [Estimated prevalence of secondary progressive multiple sclerosis in the USA and Europe: results from a systematic literature search](#). Neurology 90: (15 supplement).
4. Office of National Statistics (2017) [Population mid-year estimates](#). Accessed September 2018