NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Ponesimod for treating relapsing multiple sclerosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ponesimod within its marketing authorisation for treating relapsing forms of 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. This is characterised by more persistent or gradually increasing disability; some people with secondary progressive disease continue to have relapses.

Approximately 100,000 people in England have multiple sclerosis, and about 5,000 people are diagnosed each year.[1] Approximately 85% of people are diagnosed with relapsing–remitting multiple sclerosis and around 50% of people transition to secondary progressive multiple sclerosis within 20 years.[2-5] 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 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 relapsing–remitting multiple sclerosis:

- interferon beta-1a and glatiramer acetate for relapsing–remitting multiple sclerosis and interferon beta-1b for relapsing–remitting multiple sclerosis with 2 or more relapses within the last 2 years (NICE TA527)

- teriflunomide and dimethyl fumarate for active relapsing–remitting multiple sclerosis, only if people do not have highly active or rapidly evolving severe relapsing–remitting multiple sclerosis (NICE TA303 and TA320 respectively)

- alemtuzumab for active relapsing–remitting multiple sclerosis (NICE TA312) [1]

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

- 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)

- natalizumab for rapidly evolving severe relapsing–remitting multiple sclerosis (NICE TA127)

- cladribine tablets for treating highly active multiple sclerosis only for rapidly evolving severe relapsing–remitting disease or disease that has responded inadequately to treatment with disease-modifying therapy (NICE TA493).

Treatments for relapsing–remitting multiple sclerosis are also used for people with active secondary progressive multiple sclerosis, as evidenced by relapses. NICE technology appraisal guidance 527 recommends interferon beta-1b for treating secondary progressive multiple sclerosis in people with continuing relapses.

The technology

Ponesimod (Brand name unknown, Janssen) is a selective sphigosine-1 phosphate type 1 (S1P-1) receptor modulator and can be classed as an immunomodulatory drug. Ponesimod acts by preventing lymphocytes from crossing the blood-brain barrier into the central nervous system and causing damage to the myelin sheath around nerve cells. It is administered orally.

Ponesimod does not currently have a marketing authorisation in the UK for treating relapsing multiple sclerosis. It has been studied in a clinical trial in comparison with teriflunomide in adults with relapsing multiple sclerosis.

[1] In October 2019, the European Medicines Agency's pharmacovigilance risk assessment committee recommended restricting alemtuzumab to use in adults with relapsing remitting multiple sclerosis that is highly active despite adequate treatment with at least one disease-modifying therapy or if the disease is worsening rapidly with at least two disabling relapses in a year and brain-imaging showing new damage. The recommendations in NICE TA312 will be updated to reflect this in due course.

Intervention(s)	Ponesimod
Population(s)	People with relapsing multiple sclerosis

Comparators	For people with active relapsing-remitting multiple sclerosis: • beta-interferon • dimethyl fumarate • glatiramer acetate • teriflunomide • ocrelizumab • peginterferon beta-1a • ozanimod (subject to ongoing NICE appraisal) • ofatumumab (subject to ongoing NICE appraisal) For people with highly active relapsing-remitting multiple sclerosis despite previous treatment • alemtuzumab**Error! Bookmark not defined.** • cladribine tablets • fingolimod • ocrelizumab (only if alemtuzumab**Error! Bookmark not defined.** is contraindicated or otherwise unsuitable) • ozanimod (subject to ongoing NICE appraisal) • ofatumumab (subject to ongoing NICE appraisal) For people with rapidly-evolving severe relapsing-remitting multiple sclerosis • alemtuzumab**Error! Bookmark not defined.** • cladribine tablets • natalizumab • ocrelizumab (only if alemtuzumab**Error! Bookmark not defined.** is contraindicated or otherwise unsuitable) • ozanimod (subject to ongoing NICE appraisal) • ofatumumab (subject to ongoing NICE appraisal) For people with active secondary progressive multiple sclerosis (evidenced by continuing relapses): • established clinical management, including interferon beta-1b or other disease modifying therapies used outside their marketing authorisations • siponimod (subject to ongoing NICE appraisal)

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 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. 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 or comparator technologies will 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. If the evidence allows, the following subgroup of people will be considered: • people who could not tolerate previous treatment.

Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Ocrelizumab for treating relapsing–remitting multiple sclerosis (2018) NICE technology appraisal guidance 533. Review date July 2021. Beta interferons and glatiramer acetate for treating multiple sclerosis (2018) NICE technology appraisal guidance 527. Review date June 2021. Cladribine tablets for treating relapsing–remitting multiple sclerosis (2017) NICE technology appraisal guidance 493. Review date August 2019. Dimethyl fumarate for treating relapsing-remitting multiple sclerosis (2014) NICE technology appraisal guidance 320. Review date to be confirmed. Alemtuzumab for treating relapsing–remitting multiple sclerosis (2014) NICE technology appraisal guidance 312. Review date to be confirmed. Teriflunomide for treating relapsing–remitting multiple sclerosis (2014) NICE technology appraisal guidance 303. 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. **Appraisals in development (including suspended appraisals):** Ozanimod for treating relapsing-remitting multiple sclerosis. NICE technology appraisals guidance [ID1294]. Expected publication date July 2020. Peginterferon beta-1a for treating relapsing–remitting multiple sclerosis. NICE technology appraisals guidance [ID1521]. Expected publication date to be confirmed. Siponimod for treating secondary progressive multiple sclerosis [ID1304]. Expected publication date June 2020. **Related Guidelines:** Multiple sclerosis in adults (2014) NICE guideline 186. Review date to be confirmed. **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 NICE Pathways:** Multiple sclerosis (2014) NICE pathway.
Related National Policy	NHS England (2019) NHS Long Term Plan. NHS England (2017) https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf. Chapter 11. Adult specialist neurosciences services. NHS England (May 2014) Clinical commissioning policy: Disease Modifying Therapies for Patients with multiple sclerosis (MS). Department of Health and Social Care (2016) NHS Outcomes Framework 2016-2017. Domains 1-4.

References

1. Multiple Sclerosis Society (2018) MS in the UK [accessed October 2019].

2. Multiple Sclerosis Society (2019) Types of MS [accessed October 2019].

3. NHS Choices (2018) Multiple sclerosis – overview [accessed October 2019].

4. Patient.info (2018) Multiple sclerosis [accessed October 2019].

5. MS International Federation (2019) Types of MS [accessed October 2019].

