NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Diroximel fumarate for treating relapsing-remitting multiple sclerosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of diroximel fumarate within its marketing authorisation for relapsing–remitting 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 (in which people may have fewer 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.

Approximately 131,000 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 and around 50% of those people transition to secondary progressive multiple sclerosis within 20 years of diagnosis.[2] 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 relapsing–remitting multiple sclerosis:

- peginterferon beta-1a for relapsing–remitting multiple sclerosis (NICE TA624)
- cladribine tablets for 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 for active relapsing–remitting multiple sclerosis only if alemtuzumab is contraindicated or otherwise unsuitable (NICE TA533)

- 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 highly active relapsing–remitting multiple sclerosis despite treatment with at least 1 disease-modifying therapy, or for rapidly evolving severe relapsing–remitting multiple sclerosis (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)

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

The technology

Diroximel fumarate (ALK 8700, Biogen Idec) is a derivative of fumaric acid that helps prevent the degeneration of the myelin sheath of nerve fibres. It is administered orally.

Diroximel fumarate does not currently have marketing authorisation in the UK for treating relapsing–remitting multiple sclerosis. It has been studied in clinical trials as a monotherapy compared to dimethyl fumarate and in a single arm study in people with relapsing–remitting multiple sclerosis.

Intervention(s)	Diroximel fumarate
Population(s)	People with relapsing–remitting multiple sclerosis

Comparators	• beta interferon • dimethyl fumarate • glatiramer acetate • ocrelizumab (only if alemtuzumab is contraindicated or otherwise unsuitable) • ofatumumab (subject to ongoing NICE appraisal) • ozanimod (subject to ongoing NICE appraisal) • peginterferon beta-1a • ponesimod (subject to ongoing NICE appraisal) • teriflunomide.

Outcomes	The outcome measures to be considered include: • relapse rate • severity of relapse • disability (for example, the expanded disability status scale [EDSS]) • disease progression • symptoms of multiple sclerosis (such as fatigue, cognition and visual disturbance) • subclinical disease activity (for example, MRI outcomes) • 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 patient access schemes for the intervention or comparator technologies should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If the evidence allows, the following subgroups of people will be considered: • people who could not tolerate previous treatment.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Peginterferon beta-1a for treating relapsing–remitting multiple sclerosis (2020). NICE technology appraisal guidance 624. Review date July 2023. Cladribine tablets for treating relapsing–remitting multiple sclerosis (2017). NICE technology appraisal guidance 616.

	Review date 2022. 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. 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). Updated March 2020. Teriflunomide for treating relapsing–remitting multiple sclerosis (2014). NICE technology appraisal guidance 303. 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)** Autologous haematopoietic stem cell transplantation for treating multiple sclerosis. NICE technology appraisals guidance [ID1111]. (suspended) Laquinimod for treating relapsing-remitting multiple sclerosis. NICE technology appraisals guidance [ID560]. (suspended) Ofatumumab for treating relapsing multiple sclerosis. NICE technology appraisals guidance [ID1677]. Expected publication date TBC. Ozanimod for treating relapsing multiple sclerosis. NICE technology appraisals guidance [ID1294]. Expected publication date March 2021. Ponesimod for treating relapsing multiple sclerosis. NICE technology appraisals guidance [ID1393]. Expected publication date TBC. **Related Guidelines:** Multiple sclerosis in adults (2014). NICE guideline 186. Review date July 2022. **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 (2020) NICE pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Chapter 11. Adult specialist neurosciences services https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf NHS England (March 2019) Clinical commissioning policy: Disease Modifying Therapies for Patients with multiple sclerosis (MS) 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

References

1. Public Health England (2020) Multiple sclerosis: prevalence, incidence and smoking status - data briefing. Accessed July 2020.

2. Multiple Sclerosis Trust (2017) Secondary progressive multiple sclerosis. Accessed May 2020.