NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Fingolimod for treating relapsing multiple sclerosis in children and young people

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of fingolimod within its marketing authorisation for treating relapsing multiple sclerosis in children and young people.

Background

Multiple sclerosis is a chronic, neurodegenerative disorder 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 with variable severity and 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.

Approximately 160 people aged between 10 and 19 years in the UK have multiple sclerosis, and about 50 people are diagnosed each year[1]. Almost all children (98 in every 100) who have been diagnosed with multiple sclerosis have a type called relapsing-remitting multiple sclerosis[2]. It is characterised by periods of remission (when symptoms are mild or disappear altogether) followed by relapses (which may or may not result in residual disability). Younger people tend to experience higher frequency of relapses and greater disability compared to adults with 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. Most are used outside of the constraints of the relevant marketing authorisation in children and young people. These agents include beta interferon and glatiramer acetate which are not currently recommended by NICE (technology appraisal guidance 32, currently being reviewed), but were available in the NHS through a risk-sharing scheme; this scheme has now ended and a clinical commissioning policy is in place.

The technology

Fingolimod (Gilenya, Novartis) is a sphingosine-1-phosphate receptor (S1-PR) ligand and can be classed as immunomodulatory drug. Fingolimod acts by trapping T-cells from the bloodstream into lymph nodes, preventing T-cells from crossing the blood–brain barrier and causing damage to myelin. It is given orally.

Fingolimod does not currently have a marketing authorisation in the UK for the treatment of multiple sclerosis in children and young people. It is being studied in a clinical trial, compared with interferon beta-1a, in people aged between 10 and 17 with relapsing multiple sclerosis. Fingolimod has a marketing authorisation in the UK for the treatment of highly active relapsing remitting multiple sclerosis in adults.

Intervention(s)	Fingolimod
Population(s)	Children and young people with relapsing multiple sclerosis
Comparators	Disease-modifying therapies including treatments used outside of their marketing authorisation (such as beta interferon [subject to ongoing NICE appraisal], glatiramer acetate [subject to ongoing NICE appraisal] or natalizumab if used outside of the constraints of the relevant marketing authorisation in children and young people)
Outcomes	The outcome measures to be considered include: • relapse rate • severity of relapse • disability (for example, expanded disability status scale [EDSS]) • symptoms of multiple sclerosis such as fatigue, cognition and visual disturbance • freedom from disease activity • 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 generic or biosimilars should be taken into account. The availability of any patient access schemes 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.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Cladribine for the treatment of relapsing-remitting multiple sclerosis (2017) NICE technology appraisal guidance 493. Review date December 2020. Daclizumab for treating relapsing–remitting multiple sclerosis (2017). NICE technology appraisal guidance 441. Review date April 2020. 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. Beta interferon and glatiramer acetate for the treatment of multiple sclerosis (2002). NICE technology appraisal guidance 32. Review ongoing, publication date to be confirmed. **Appraisals in development (including suspended appraisals)** Ocrelizumab for treating relapsing multiple sclerosis. NICE technology appraisal guidance [ID937]. Expected publication July 2018. Multiple sclerosis - interferon beta, glatiramer acetate (review TA32). NICE technology appraisal guidance [ID809]. Publication date to be confirmed. Laquinimod for treating relapsing-remitting multiple sclerosis. NICE technology appraisal guidance [ID560] (suspended). **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 (2017) Commissioning Medicines for Children in Specialised Services. Clinical commissioning policy reference 170001/P Department of Health (2016) NHS outcomes framework 2016 to 2017: Domains 1–5. NHS England (2016) Manual for Prescribed Specialised Services 2016/17. Chapter 11. Adult specialist neurosciences services NHS England (2014) Disease Modifying Therapies for Patients with multiple sclerosis (MS). Clinical commissioning policy reference D04/P/b.

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for multiple sclerosis for children and young people?

Have all relevant comparators for fingolimod been included in the scope?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom fingolimod is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider fingolimod will fit into the existing NICE pathway, multiple sclerosis?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which fingolimod will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider fingolimod to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of fingolimod can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Multiple Sclerosis Society (2016) MS in the UK [accessed December 2017].

2. Renoux et al. (2007). Natural history of multiple sclerosis with childhood onset. New England Journal of Medicine, 356(25), 2603-2613.

