NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Siponimod for treating secondary progressive multiple sclerosis

Draft scope (pre-referral)

Draft 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 (MS) is a chronic, neurodegenerative disorder that 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. Relapsing-remitting multiple sclerosis (RRMS) is the most common clinical form of MS, characterised by periods of remission followed by relapse (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 with fewer or no relapses.[1]

Approximately 110,000 people in the UK have MS, with 5,000 people diagnosed each year.[2] Approximately 85% of people are diagnosed with the RRMS form and 50% of people transition from RRMS to SPMS within 20 years.[3] There are an estimated 38,000 people in the UK with SPMS. [4, 5]

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 (BAF-312, Novartis) is a selective agonist of the sphingosine-1 phosphate (S1P) receptors 1 and 5. The drug selectively binds to circulating lymphocytes which enables a reversible trapping of a proportion of lymphocytes in 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	• Best supportive care For people with active disease, evidenced by relapses: • Interferon beta 1b
Outcomes	The outcome measures to be considered include: • 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 • 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 of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. For the comparator, the availability and cost of biosimilars 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 and NICE Pathways	**Related Technology Appraisals:** 'Beta-interferons and glatiramer acetate for treating multiple sclerosis' (2018). NICE Technology Appraisal 527. Review date June 2021. **Appraisals in development (including suspended appraisals)** 'Biotin for treating primary and secondary progressive multiple sclerosis' NICE technology appraisals guidance [ID919]. Publication date to be confirmed (suspended appraisal) **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. Review date January 2019. **Related Quality Standards:** Multiple sclerosis (2016) NICE quality standard QS108. **Related NICE Pathways:** Multiple sclerosis (2014) NICE pathway.
Related National Policy	NHS England (2014) Disease modifying therapies for patients with Multiple Sclerosis. NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Chapter 11. Adult specialist neurosciences services. Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1-5.

Questions for consultation

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

Which treatments are considered to be established clinical practice in the NHS for secondary progressive multiple sclerosis?

What proportion of people with secondary progressive multiple sclerosis no longer has relapses?

How should best supportive care be defined? Does this differ depending on whether the person has ongoing relapses or not?

Are the outcomes listed appropriate?

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

Where do you consider siponimod 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 siponimod 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 siponimod 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 siponimod 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Multiple Sclerosis Trust (2018) MS: the facts. Accessed September 2018
2 Multiple Sclerosis Trust (2018) Prevalence and incidence of multiple sclerosis. Accessed September 2018.
3 Multiple Sclerosis Trust (2017) Secondary progressive multiple sclerosis. Accessed September 2018
4 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).
5 Office of National Statistics (2017) Population mid-year estimates. Accessed September 2018