

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Fingolimod for the treatment of primary progressive multiple sclerosis

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of fingolimod within its licensed indications for the treatment of primary progressive multiple sclerosis.

Background

Multiple sclerosis (MS) is a chronic, disabling neurological disease. It occurs when the body's immune system attacks myelin, a protective sheath around nerve fibres in the brain and spinal cord, which ensures that nerves transmit electrical impulses efficiently. Damage to the myelin causes nerve impulses to be slowed or distorted. In addition to myelin loss, the nerve fibres, themselves, are also damaged.

MS has an unpredictable course with variable severity and rates of progression. Symptoms include weakness, chronic fatigue, unsteady gait, speech problems, incontinence and cognitive impairment. Relapses can have a highly debilitating impact on quality of life to the extent that they may require hospitalisation, and be associated with significant disability and incapacity; however, many people with MS have little or no disability, and are able to lead normal working lives.

Three main clinical forms of MS are defined, based on their respective patterns of the disease. In relapsing-remitting MS (RRMS), periods of remission are followed by relapses; this affects 80% of people at disease onset. The majority of these people will develop secondary progressive MS (SPMS) – some within the first 10 years – where there are gradually more or worsening symptoms with fewer remissions. Primary progressive MS (PPMS) is a form of the disease which progresses inexorably, affecting 10 to 15% of people at disease onset.

MS is the most common cause of neurological disability in young adults between the ages of 20 and 40 years. Onset of the disease is usually in early adulthood, and occurs roughly twice as often in women as in men. The exact prevalence of MS is unknown, but it has been estimated that 85,000 people in the UK have MS, with 2500 new cases diagnosed each year. Within England, approximately 6200 people have PPMS. The effect of MS on life expectancy is uncertain, it has been estimated that people with MS have life expectancy 7 years shorter than the general population

There are no curative therapies available for MS. There are currently no licensed pharmacological treatments for the management of PPMS.

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Symptoms of PPMS may be managed with physiotherapy, occupational therapy and speech therapy.

The technology

Fingolimod (FTY720, Novartis) is in a class of immunomodulatory drugs (sphingosine 1-phosphate receptor (S1-PR) modulators). Fingolimod is thought to directly reduce neurodegeneration and enhance repair of CNS damage by interacting with S1-PRs expressed on brain cells. In addition, fingolimod is thought to exert lymphocyte-mediated anti-inflammatory effects. It is given orally.

Fingolimod does not currently have a UK marketing authorisation. It has been studied in clinical trials in comparison with placebo for use in adults with PPMS. It is also being studied for treatment of RRMS.

Intervention(s)	Fingolimod
Population(s)	Adults with primary progressive multiple sclerosis
Comparators	Standard care with no disease-modifying treatment
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • mortality • disability progression • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.

<p>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No. 127, Aug 2007, 'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis.'</p> <p>Technology Appraisal No. 32, Jan 2002, 'Multiple sclerosis – beta interferon and glatiramer acetate.'</p> <p>Related Guidelines:</p> <p>Clinical Guideline No. 38, Nov 2003, 'Management of multiple sclerosis in primary and secondary care.'</p>
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Questions for consultation

Has the most appropriate comparator for the treatment of primary progressive multiple sclerosis been included in the scope? Are there any other interventions used to treat PPMS that would be appropriate comparators of fingolimod?

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

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)