NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Fingolimod for the treatment of relapsing-remitting multiple sclerosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of fingolimod within its licensed indication for the treatment of relapsing-remitting 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, which can lead to irreversible damage.

MS has an unpredictable course with variable severity and rates of progression. Symptoms include weakness, chronic fatigue, unsteady gait, speech problems, incontinence, visual disturbance and cognitive impairment. MS can have a debilitating impact on quality of life, particularly during relapses, which may require hospitalisation, and be associated with significant disability and incapacity. Many people with MS have little or no disability during periods of remission in the early stages of disease; recoveries from relapses lessen as the disease progresses.

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, briefer remissions (or none at all) and a progressive increase in disability. 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 at least twice as often in women as in men. The exact prevalence of MS is unknown, but it has been estimated that 100,000 people in the UK currently have MS, with 2500 new cases diagnosed each year. RRMS accounts for approximately 40% of all MS cases, which equates to roughly 34,000 people in the UK. 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. Current pharmacological management of RRMS includes the use of disease modifying agents, such as interferon beta, glatiramer acetate, and natalizumab, targeted at reducing the frequency and/or severity of relapses and/or slowing the course of disease progression. Interferon beta and glatiramer acetate are not currently recommended by NICE (Technology Appraisal Guidance 32), but are available in the NHS through a Risk Sharing Scheme. NICE recommends natalizumab as an option for the treatment only of rapidly evolving severe RRMS (Technology Appraisal Guidance 127). Corticosteroids are also sometimes used for managing relapses. Symptoms of MS may also be managed with physiotherapy, occupational therapy and speech therapy.

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 UK marketing authorisation. It has been studied in clinical trials in comparison with either placebo or beta-1a interferon as first- and subsequent-line therapy for adults with RRMS. It is also being studied for treatment of PPMS.

Intervention(s)	Fingolimod
Population(s)	Adults with relapsing-remitting multiple sclerosis
Comparators	• Interferon beta • Glatiramer acetate • Optimised standard care with no disease-modifying treatment In addition, for people with rapidly evolving severe relapsing-remitting multiple sclerosis: • Natalizumab

Outcomes	The outcome measures to be considered include: • relapse rate • disability progression • disease activity (including symptoms such as fatigue, cognition and visual disturbance) • 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. Arrangements within the risk-sharing scheme, which was agreed for the supply of disease modifying treatments for Multiple Sclerosis in the NHS (see Health Service Circular 2002/004), may be taken into consideration in the economic evaluation where these are relevant to the appraisal of fingolimod.
Other considerations	If evidence allows, consideration will be given to subgroups defined by prior treatment. Consideration should be given to the possible impact of fingolimod being an oral preparation. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 127, August 2007, 'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis.' Review date June 2010. Technology Appraisal No. 32, January 2002, 'Multiple sclerosis – beta interferon and glatiramer acetate.' Static guidance. NICE technology appraisal in preparation, 'Cladribine for the treatment of relapsing-remitting multiple sclerosis.' Earliest anticipated date of publication to be confirmed. NICE technology appraisal in preparation. 'Fingolimod for the treatment of primary progressive multiple sclerosis.' Earliest anticipated date of publication to be confirmed. Related Guidelines: Clinical Guideline No. 38, Nov 2003, 'Management of multiple sclerosis in primary and secondary care.' Review date November 2010.