

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Cladribine for the treatment of relapsing-remitting multiple sclerosis

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of cladribine 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.

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 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 beta interferon, glatiramer acetate, and natalizumab, targeted at reducing the frequency and/or severity of relapses and/or slowing the course of disease progression. Beta interferon 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). Mitoxantrone and corticosteroids are also sometimes used for the treatment of RRMS. Symptoms of MS may also be managed with physiotherapy, occupational therapy and speech therapy.

The technology

Cladribine (Movectro, Merck Serono) is thought to reduce autoimmune destruction of myelin via anti-lymphocytic effects (it is a deaminase-resistant deoxyadenosine analogue that selectively reduces lymphocyte counts). It is anticipated that cladribine will be given orally for the treatment of RRMS.

Cladribine does not have a UK marketing authorisation for multiple sclerosis. It is being studied in clinical trials for use in patients with RRMS in comparison with placebo for initial treatment and retreatment of RRMS. It is also being studied in combination with beta interferon compared with beta interferon alone (that is, as an add-on therapy) in adults who have experienced at least one relapse whilst receiving beta interferon during the previous 48 weeks. Cladribine has a UK marketing authorisation for the treatment of leukaemia.

Intervention(s)	Cladribine alone or in combination with beta interferon
Population(s)	Adults with relapsing-remitting multiple sclerosis
Comparators	<p>For cladribine as add-on therapy to beta interferon:</p> <ul style="list-style-type: none"> • beta interferon <p>For cladribine monotherapy:</p> <ul style="list-style-type: none"> • beta interferon • glatiramer acetate • mitoxantrone • standard care with no disease-modifying treatment <p>In addition, for people with rapidly evolving severe relapsing-remitting multiple sclerosis:</p> <ul style="list-style-type: none"> • natalizumab

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • mortality • relapse rate • disability progression • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>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 cladribine.</p>
Other considerations	<p>If the evidence allows, subgroups by prior treatment with beta interferon will be considered.</p> <p>Guidance will only be issued in accordance with the marketing authorisation.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>Technology appraisal No. 127, August 2007, 'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis.'</p> <p>Technology appraisal No. 32, January 2002, 'Multiple sclerosis – beta interferon and glatiramer acetate.' January 2002.</p> <p>Related Guidelines:</p> <p>Clinical guideline No. 38, November 2003, 'Management of multiple sclerosis in primary and secondary care.'</p>

Questions for consultation

Have the most appropriate comparators for the treatment of relapsing-remitting multiple sclerosis been included in the scope? Are the comparators listed routinely used in clinical practice?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other 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)