NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Laquinimod for treating relapsing-remitting multiple sclerosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of laquinimod within its licensed indication for treating relapsing-remitting multiple sclerosis.

Background

Multiple sclerosis (MS) is a chronic, neurodegenerative disorder with multifocal inflammatory demyelination affecting the brain, optic nerves, and spinal cord and this process leads in most patients to progressive neurological impairment and severe disability. Approximately 100,000 people in the UK have MS, and about 2500 people are newly diagnosed each year.

Relapsing-remitting MS (RRMS) is one clinical form of MS which affects approximately 80% of people at time of diagnosis. It is characterised by periods of remission followed by relapses (which may or may not result in underlying disability). Most people with RRMS will develop secondary progressive MS (SPMS). Around 65% of people with RRMS develop SPMS within 15 years of diagnosis. SPMS is characterised by more persistent or gradually increasing disability. Some people with SPMS may still experience relapses. MS 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.

There is no cure for MS. Current pharmacological management of RRMS includes the first-line use of disease-modifying agents to reduce the frequency and severity of relapses. These include beta interferon and glatiramer acetate which are not currently recommended by NICE (technology appraisal guidance 32), but are available in the NHS through a risk-sharing scheme. For people with rapidly-evolving severe RRMS, natalizumab is recommended (NICE technology appraisal guidance 127). In clinical practice, another beta interferon or glatiramer acetate, or a dose escalation of existing beta interferon treatment may be administered as a second-line treatment for people whose disease has had an inadequate response to their first treatment. NICE has also recommended fingolimod as an option for the treatment of highly active RRMS in adults who have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon (NICE technology appraisal guidance 254).

The technology

Laquinimod (Nerventra, Teva UK) is a synthetic immune modulator with anti-inflammatory and neuroprotective properties. It is administered orally.

Laquinimod does not currently have a UK marketing authorisation for the treatment of RRMS. It has been studied in adults with RRMS as monotherapy compared with either placebo or beta interferon-1a.

Intervention(s)	Laquinimod
Population(s)	People with relapsing-remitting multiple sclerosis
Comparators	• beta-interferon • glatiramer acetate • teriflunomide • natalizumab (for patients with rapidly-evolving severe relapsing-remitting multiple sclerosis) • fingolimod (for patients with highly active relapsing-remitting multiple sclerosis who have received treatment with beta interferon)
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 of 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 patient access schemes for the intervention or comparator technologies should be taken into account. This includes the 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).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If the evidence allows, the following subgroups of patients will be considered: • patients with relapsing-remitting multiple sclerosis who have received no prior treatment (treatment naïve) • patients with relapsing-remitting multiple sclerosis who have received prior treatment (treatment experienced) • patients with highly active relapsing-remitting multiple sclerosis • patients with rapidly evolving severe relapsing-remitting multiple sclerosis In order to align with clinical practice, the sensitivity of the cost effectiveness of laquinimod to including more than 1 disease modifying treatment in the treatment pathway will be considered. For the external validation of the modelling, the similarity of the cost effectiveness estimates for current active treatments (all beta interferons and glatiramer acetate) compared with no treatment in the NHS risk-sharing scheme for multiple sclerosis will be considered.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 32, January 2002, 'Multiple sclerosis – beta interferon and glatiramer acetate'. Static guidance. Technology Appraisal No. 127, August 2007, 'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis'. Review proposal date 2013 (will be reviewed alongside TA32 and TA127). Technology Appraisal No. 254, April 2012, 'Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis'. Review proposal date 2013 (will be

	reviewed alongside TA32 and TA127). Technology Appraisal in Preparation, 'Cladribine for the treatment of relapsing-remitting multiple sclerosis'. Suspended. Technology Appraisal in Preparation, 'Alemtuzumab for treating relapsing-remitting multiple sclerosis'. Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, 'Dimethyl fumarate for treating relapsing-remitting multiple sclerosis'. Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, 'Teriflunomide for treating relapsing-remitting multiple sclerosis'. Earliest anticipated date of publication January 2014. Related Guidelines: Clinical Guideline No. 8, November 2003, 'Management of multiple sclerosis in primary and secondary care'. Review in preparation. Earliest anticipated date of publication 2014.