NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Alemtuzumab for the treatment of relapsing-remitting multiple sclerosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of alemtuzumab within its licensed indication for the treatment of 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 disease onset. It is characterised by periods of remission followed by relapses (which may or may not result in residual disability). Most people with RRMS will develop secondary progressive MS (SPMS), and around 65% develop it within 15 years of diagnosis. SPMS is characterised by more persistent or gradually progressive disability. 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 (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 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 relapsing–remitting multiple sclerosis 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

Alemtuzumab (Lemtrada, Genzyme (a Sanofi company)) selectively decreases auto-immune reaction by binding to the CD52 antigen on B and T lymphocytes and monocytes, initiating cell lysis and reducing their circulating numbers. It is administered by intravenous infusion over 5 days in the first year of treatment, and over 3 days in the second year of treatment.

Alemtuzumab does not currently have a UK marketing authorisation for the treatment of RRMS. It has been studied in clinical trials as monotherapy in comparison with beta-interferon in adults with RRMS. One trial was for treatment-naïve patients and another for those who had relapsed on previous treatment.

Intervention	Alemtuzumab
Population	People with relapsing-remitting multiple sclerosis
Comparators	• beta-interferon • glatiramer acetate • natalizumab (for treatment-naïve or previously treated 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 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 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: • treatment experienced patients with relapsing-remitting multiple sclerosis • treatment naïve patients with relapsing-remitting multiple sclerosis • patients with highly active relapsing-remitting multiple sclerosis whose disease has inadequately responded to or are intolerant to treatment with disease modifying therapy • patients with rapidly evolving severe relapsing-remitting multiple sclerosis
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. Technology Appraisal No. 254, Apr 2012, 'Fingolimod

	for the treatment of highly active relapsing-remitting multiple sclerosis'. Review date TBC (will be reviewed alongside TA127 and TA32). Technology Appraisal in development, 'Dimethyl fumarate for the treatment of relapsing-remitting multiple sclerosis' Expected date of publication: January 2014. Technology Appraisal in development, 'Teriflunomide for the first line treatment of relapsing-remitting multiple sclerosis'. Expected date of publication: January 2014. Technology Appraisal in development, 'Laquinimod for the treatment of relapsing-remitting multiple sclerosis'. Expected date of publication: February 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.