# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Single Technology Appraisal

## Alemtuzumab for the treatment of relapsing-remitting multiple sclerosis

## Draft 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 increasing disability, and 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 (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) 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.

Alemtuzumab does not currently have a UK marketing authorisation for the treatment of RRMS. It has been studied in clinical trials as a 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<br>• glatiramer acetate<br>• natalizumab (for patients with rapidly-evolving severe relapsing-remitting multiple sclerosis)<br>• 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:<br>• relapse rate<br>• severity of relapse<br>• disability (for example, expanded disability status scale [EDSS])<br>• symptoms of multiple sclerosis (such as fatigue, cognition and visual disturbance)<br>• mortality<br>• adverse effects of treatment<br>• 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.<br><br>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.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>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<br><br>If the evidence allows, the following subgroups of patients will be considered:<br><br>• patients with relapsing-remitting multiple sclerosis whose disease has inadequately responded to or are intolerant to treatment with disease modifying therapy<br><br>• patients with highly active relapsing-remitting multiple sclerosis<br><br>• patients with rapidly evolving severe relapsing-remitting multiple sclerosis |
| **Related NICE recommendations** | Related Technology Appraisals:<br><br>Technology Appraisal No. 32, January 2002, 'Multiple sclerosis – beta interferon and glatiramer acetate'. Static guidance.<br><br>Technology Appraisal No. 127, August 2007, 'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis'. Review proposal date 2013.<br><br>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). |

| | |
|---|---|
| | Proposed Technology Appraisal, 'Dimethyl fumarate for the treatment of relapsing-remitting multiple sclerosis'.<br><br>Proposed Technology Appraisal, 'Laquinimod for the treatment of relapsing-remitting multiple sclerosis'.<br><br>Proposed Technology Appraisal, 'Teriflunomide for the first line treatment of relapsing-remitting multiple sclerosis'.<br><br>Related Guidelines:<br><br>Clinical Guideline No. 8, November 2003, 'Management of multiple sclerosis in primary and secondary care'. Review in preparation. Earliest anticipated date of publication 2014. |

## Questions for consultation

Has the population for alemtuzumab for treating multiple sclerosis been defined appropriately?

Have the most appropriate comparators for alemtuzumab for treating RRMS been included in the scope? Are the comparators listed routinely used in clinical practice?

Should best supportive care be included as a comparator?

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

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which alemtuzumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider alemtuzumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of alemtuzumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.