# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Health Technology Appraisal

## Natalizumab for the treatment of multiple sclerosis

## Final Scope

### Remit/appraisal objective

To appraise the clinical and cost effectiveness of natalizumab in its licensed indications for the treatment of multiple sclerosis, and to provide guidance to the NHS in England and Wales[1].

### 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 myelin causes nerve impulses to be slowed or distorted. In addition to myelin loss, there is damage to the actual nerve fibres.

MS has an unpredictable course with a variable severity and progression rate. Symptoms include weakness, chronic fatigue, unsteady gait, speech problems, incontinence and cognitive impairment. Relapses may require hospitalisation, and be associated with significant disability and incapacity, and have a highly debilitating impact on quality of life. Many people with MS, however, have little or no disability and are able to lead a normal working life.

Three main clinical forms of MS are defined, based on the pattern 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 where the disease progresses inexorably from onset (affecting 10 to 15% of people at disease onset).

The exact prevalence of MS is unknown but studies suggest that the prevalence rate in England and Wales is between 100 and 120 per 100,000. The annual incidence is estimated to be 3 to 7 per 100,000 and it is the most common cause of neurological disability in young adults between 20-40 years of age. MS usually begins in early adult life, and occurs in around twice as many women as men.

[1]DH Remit: To prepare a technology appraisal on the clinical and cost effectiveness of natalizumab for the treatment of multiple sclerosis

There are no curative therapies available for MS. Current pharmacological management for RRMS and SPMS includes the use of disease modifying agents, such as beta interferon and glatiramer acetate, targeted at reducing the frequency and/or severity of relapses and/or slowing the course of disease progression. Beta interferon and glatiramer acetate have been supplied under a risk-sharing scheme, which has been designed to ensure that they are provided cost-effectively to the NHS. Mitoxantrone is also sometimes used for treatment of active forms of RRMS or SPMS. In addition, symptoms of MS are managed with non-pharmacological techniques such as physiotherapy, occupational therapy and speech therapy.

**The technology**

Natalizumab (Tysabri, Biogen Idec), a monoclonal antibody, is a novel disease modifying agent belonging to a new class of therapies called selective adhesion molecule inhibitors. It is thought to act by inhibiting the migration of leukocytes into the central nervous system, hence reducing inflammation and demyelination.

Natalizumab has a marketing authorisation as single disease modifying therapy in highly active RRMS for the following patient groups: 1) patients with high disease activity despite treatment with a beta interferon, and 2) patients with rapidly evolving severe RRMS. Natalizumab is not licensed for use in combination with a beta interferon or glatiramer acetate.

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| **Intervention** | Natalizumab |
| **Population** | Adults with highly active RRMS who have:<br>• high disease activity despite treatment with a beta interferon, or<br>• rapidly evolving severe RRMS |
| **Standard comparators** | For adults with RRMS and high disease activity despite treatment with a beta interferon:<br>• glatiramer acetate and mitoxantrone<br>• standard care with no disease modifying treatment<br>For adults with rapidly evolving severe RRMS:<br>• beta interferon, glatiramer acetate and mitoxantrone<br>• standard care with no disease modifying treatment |

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| **Outcomes** | The outcome measures to be considered include:<br>• mortality<br>• relapse rate<br>• disability progression<br>• adverse effects of treatment, including progressive multifocal leukoencephalopathy<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>The time horizon for the economic evaluation should reflect the chronic nature of the condition.<br>Where evidence for head to head comparisons with relevant comparators is not available, appropriate methods for indirect comparison should be used.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>Arrangements within the risk-sharing scheme, which was agreed for the supply of disease modifying treatments for Multiple Sclerosis on 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 natalizumab. |
| **Other considerations** | If the evidence allows, the appraisal will attempt to identify criteria for selecting patients for whom natalizumab would be particularly appropriate.<br>The intervention will be appraised according to its marketing authorisation. |
| **Related NICE recommendations** | Related Technology Appraisals:<br>NICE Technology Appraisal Guidance No. 32. - Beta interferon and glatiramer acetate for the treatment of multiple sclerosis (2002).<br>Related Guidelines:<br>NICE Clinical Guideline No. 8 - Management of multiple sclerosis in primary and secondary care (2003). |