NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Teriflunomide for the treatment of relapsing forms of multiple sclerosis

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of teriflunomide, within its licensed indication, for the treatment of relapsing forms of 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. Approximately 100,000 people in the UK have MS, and about 2500 people are newly diagnosed each year. Relapsing-remitting MS (RRMS) is characterised by periods of remission followed by relapses, and accounts for approximately 40% of the MS population. Most people with RRMS develop secondary progressive MS (SPMS), around 65 per cent of people with RRMS will develop SPMS 15 years after being diagnosed. SPMS is characterised by increasing disability, and although some people with SPMS still experience periods of remittance, they do not tend to recover completely from a relapse. MS can have a debilitating impact on quality of life, particularly during relapses, which may require hospitalisation, and be associated with significant disability and incapacity.

No curative therapies are available for MS. Current pharmacological management includes the use of disease modifying agents targeted at reducing the frequency and/or severity of relapses and/or slowing the course of disease progression. These include interferon beta 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 developed by the Department of Health. Also natalizumab is an option for the treatment of rapidly-evolving severe RRMS (Technology Appraisal Guidance 127). Symptoms of MS may also be managed with physiotherapy, occupational therapy and speech therapy.

Recently, fingolimod has received a UK marketing authorisation for the treatment of relapsing-remitting multiple sclerosis and is currently being appraised by NICE.

The technology

Teriflunomide (Aubagio, Sanofi) is an oral, immunomodulatory, disease-modifying agent with anti-inflammatory properties. It inhibits dihydroorotate

dehydrogenase which results in blocking the proliferation and functioning of activated T and B lymphocytes, which are thought to damage myelin. Teriflunomide does not affect slowly dividing or resting lymphocytes, thereby maintaining the patient's immune system's response to infection.

Teriflunomide does not currently have a UK marketing authorisation for treatment of RRMS. It has been studied in clinical trials for adults with RRMS in comparison with placebo and in comparison with interferon beta. It has also been studied in a clinical trial compared with placebo in MS patients who experience relapses (relapsing-remitting, secondary progressive or progressive relapsing). A clinical trial comparing teriflunomide with placebo for patients who are treated with interferon beta will report in 2014.

Intervention(s)	Teriflunomide
Population(s)	Adults with relapsing-remitting or secondary progressive multiple sclerosis who experience relapses
Comparators	• beta interferon • glatiramer acetate • fingolimod (subject to NICE appraisal) • standard care with no disease-modifying treatment
Outcomes	The outcome measures to be considered include: • relapse rate • disability progression • disease activity (including symptoms such as fatigue, cognition and visual disturbance) • 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. 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 fingolimod.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 127, Aug 2007, 'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis.' Review date Jun 2010. Technology Appraisal No. 32, Jan 2002, 'Multiple sclerosis – beta interferon and glatiramer acetate.' Static list Technology Appraisal in Preparation, 'Fingolimod for the treatment of relapsing-remitting multiple sclerosis.' Earliest anticipated date of publication April 2012 Technology Appraisal in Preparation, 'Cladribine for the treatment of relapsing-remitting multiple sclerosis.' Suspended. Clinical Guideline No. 8, Nov 2003, 'Management of multiple sclerosis in primary and secondary care.' Review in preparation. Earliest anticipated date of publication tbc.

Questions for consultation

Is the definition of the population appropriate?

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

Are there any subgroups of people in whom the technology 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 [the treatment(s)] is/are/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 the technology 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 the technology 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

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)