NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Sativex as an add-on treatment of moderate to severe spasticity in multiple sclerosis

Revised Draft Scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of Sativex within its licensed indication as an add-on treatment of moderate to severe spasticity in multiple sclerosis.

Background

Multiple sclerosis 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 the myelin causes nerve impulses to be slowed or distorted. In addition to myelin loss, the nerve fibres, themselves, are also damaged, which can lead to irreversible disability.

Multiple sclerosis is a common cause of neurological disability in young adults between the ages of 20 and 40 years. Onset of the disease is usually in early adulthood, and occurs roughly twice as often in women as in men. The exact prevalence of multiple sclerosis is unknown, but it has been estimated that 100,000 people in the UK currently have multiple sclerosis, with 2500 new cases diagnosed each year.

Multiple sclerosis has an unpredictable course with variable severity, rates of progression and rates of relapse. Symptoms include chronic fatigue, speech problems, incontinence and cognitive impairment. Spasticity (altered muscle tone in the limbs) and spasms are common in people with multiple sclerosis and may be the dominant disabling impairment in some people causing reduced mobility. These impairments can also cause pain and distress. It is estimated that approximately 60% of people with multiple sclerosis have symptoms of spasticity.

There is no curative therapy for multiple sclerosis. Treatment focuses on symptom relief, reducing the severity and frequency of relapses and slowing the progression of disease. NICE clinical guideline No. 8 ('Diagnosis and management of multiple sclerosis in primary and secondary care') recommends that initially, advice should be given on physical techniques, such as passive stretching, to reduce spasticity and avoid the development of contractures. The initial pharmacological treatment for spasticity or spasms should be with baclofen or gabapentin. If these drugs are unsuccessful or cannot be tolerated, tizanidine, diazepam, clonazepam or dantrolene may be

tried. The guideline states that intramuscular botulinum toxin should not be used routinely, but can be considered for relatively localised spasticity or spasticity that has not responded to other treatments.

The technology

Sativex (an oromucosal spray containing 38-44 mg and 35-42 mg of two extracts (as soft extracts) from Cannabis sativa L., folium cum flore (Cannabis leaf and flower) corresponding to 27 mg delta-9-tetrahydrocannabinol and 25 mg cannabidiol, GW Pharma/Bayer Healthcare) contains two extracts (as soft extracts) from cannabis leaf and flower corresponding to delta-9-tetrahydrocannabinol and cannabidiol.

Sativex has a marketing authorisation in the UK and is indicated as add-on treatment, for symptom improvement in patients with moderate to severe spasticity due to multiple sclerosis whose condition has not responded adequately to other anti-spasticity medication and whose condition has demonstrated clinically significant improvement in spasticity related symptoms during an initial trial of therapy.

Intervention(s)	Sativex (38-44 mg and 35-42 mg of two extracts (as soft extracts) from Cannabis sativa L., folium cum flore (Cannabis leaf and flower) corresponding to 27 mg delta-9-tetrahydrocannabinol and 25 mg cannabidiol) as an add-on to anti-spasticity medication
Population(s)	Adults with moderate to severe spasticity due to multiple sclerosis whose condition has not responded adequately to other anti-spasticity medication and whose condition has demonstrated clinically significant improvement in spasticity related symptoms during an initial trial of Sativex
Comparators	Treatment with anti-spasticity medication without Sativex (such as baclofen, gabapentin and benzodiazepines)
Outcomes	The outcome measures to be considered include: • spasticity • spasm frequency • physical function (including motor function, walking ability, and activities of daily living) • quality of sleep • pain • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations	Related Technology Appraisals: Technology appraisal No. 127, August 2007, 'Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis.' Review date June 2010. Technology appraisal No. 32, January 2002, 'Multiple sclerosis – beta interferon and glatiramer acetate.' January 2002. Review date 'static' Technology appraisal in preparation. 'Cladribine for relapsing-remitting multiple sclerosis.' Earliest anticipated date of publication to be confirmed. Technology appraisal in preparation, 'Fingolimod for the treatment of relapsing-remitting multiple sclerosis.' Earliest anticipated date of publication to be confirmed. Technology appraisal in preparation. 'Fingolimod for the treatment of primary progressive multiple sclerosis.' Earliest anticipated date of publication to be confirmed. Technology appraisal in preparation. 'Fampridine for the improvement of walking ability in multiple sclerosis' Earliest anticipated date of publication to be confirmed Technology appraisal in preparation (Suspended), 'Interferon beta-1b, interferon beta-1a and glatiramer acetate for the treatment of single demyelinating event with clinically isolated syndrome.' Earliest anticipated date of publication to be confirmed. Related Guidelines:

	Clinical guideline No. 8, November 2003, 'Management of multiple sclerosis in primary and secondary care.' Review date February 2011.

Questions for consultation

With which interventions is Sativex expected to be used as an 'add-on' treatment?

In what place in the care pathway for multiple sclerosis is Sativex expected to be used?

Have the most appropriate comparators for Sativex as an add-on treatment of moderate to severe spasticity due to multiple sclerosis when the condition has not responded adequately to other anti-spasticity medication been included in the scope?

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?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

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)