APPENDIX A

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Cannabinoids for symptom relief in multiple sclerosis

Scope

Objective: to establish the clinical and cost effectiveness of cannabinoid-based products, within their licensed indications, for the management of symptoms associated with multiple sclerosis, and to produce 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 nerves transmit electrical impulses efficiently. Damage to myelin causes nerve impulses to be slowed or distorted. In addition to myelin loss, there can be damage to the actual nerve fibres, resulting in an accumulation of disability with time. It is estimated that some 63 000 people in England and Wales have MS. The annual incidence is estimated at 2–10 per 100,000 and it is the most common cause of neurological disability in the young. MS usually begins in individuals aged between 20 and 40 years, and occurs in about twice as many women as men.

Damage to the nervous system leads to a large number of symptoms that can differ greatly between patients and which have an adverse and often highly debilitating impact on the quality of life of people with MS and their families. Common problems include weakness affecting the arms and legs, spasticity, uncoordinated speech, tremor and altered sensation, including paresthesia and a feeling of burning, tearing and numbness in the limbs, trunk and face. Other problems include urinary dysfunction, constipation, abnormal eye movements, optic neuritis (pain in one eye followed by visual disturbances and, rarely, partial blindness), cognitive impairment, mood changes, depression and anxiety, sleep disturbances and sexual dysfunction.

The symptoms of MS are managed with both pharmacological and non-pharmacological techniques such as physiotherapy, occupational therapy and speech therapy.

Naturally occurring cannabis contains a group of chemical compounds called "cannabinoids". There are over 60 different cannabinoids; delta-9-tetrahydrocannabinol (THC) is one of the most abundant and is the main psychoactive agent but research into other cannabinoids is ongoing.

The technology: A number of cannabinoid preparations are under investigation for the management of symptoms associated with MS.

GW Pharmaceuticals PLC have just completed Phase III trials in the UK of a cannabis-based medicine extract (CBME) made from whole plant cannabis extracts. Its principal constituents are the cannabinoids THC and cannabidiol (CBD) in an approximately one to one ratio. It is administered as an oro-mucosal spray. Dronabinol (Marinol®, Solvay Healthcare Ltd) is a synthetic oral THC that is not licensed in the UK but is available on a

named patient basis as an anti-emetic in cancer chemotherapy and to treat anorexia in AIDS patients. The efficacy of dronabinol in the management of symptoms associated with MS has been examined in the 'Cannabinoids in Multiple Sclerosis Trial' (CAMS), which is funded by the Medical Research Council and is due to report in mid 2003.

Intervention(s)	CBME and dronabinol
Population(s)	Individuals with MS
Current standard treatments (comparators)	Pharmacological treatments to relieve the symptoms associated with MS
Other considerations:	The interventions will be appraised according to their anticipated licensed indications. If the evidence allows, the appraisal will attempt to identify the criteria for selecting patients for whom this treatment would be particularly appropriate. Any dose-related effects will be taken into consideration. Potential adverse effects, including psychological effects, should be identified. Outcome measures should include measures of symptom severity including relevant patient-focussed measures of function and quality of life. It is assumed that individuals participating in clinical trials may also be utilising non-pharmacological strategies. Where the evidence permits this will be taken into consideration. Publication of guidance is subject to a UK marketing authorisation being issued for one or both of the products featured in this appraisal.

[1] The remit from the Department of Health/Welsh Assembly Government was "To assess the clinical and cost effectiveness of cannabis derivatives for symptom relief in patients with multiple sclerosis relative to generally used existing therapies"