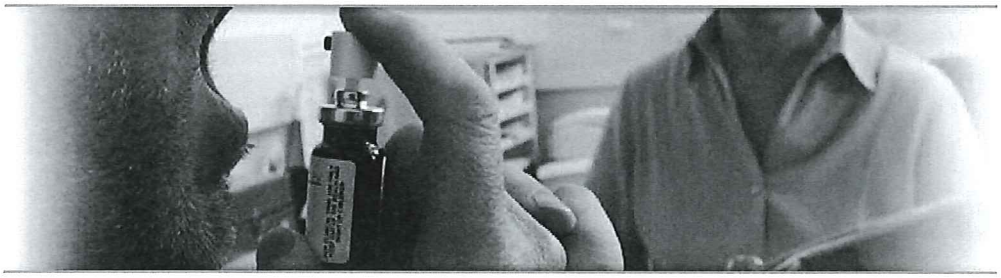
# Multiple Sclerosis

*Multiple Sclerosis (MS) is the most common disabling neurological condition affecting young adults. According to the World Health Organization, MS affects more than 1.3 million people worldwide, of which over 400,000 are in the United States and over 600,000 are in Europe. MS affects twice as many women as men and typically develops between the ages of 20 and 40 years.*

People with MS suffer from a range of symptoms, including pain, muscle spasticity and spasm, bladder problems and sleep disturbance.

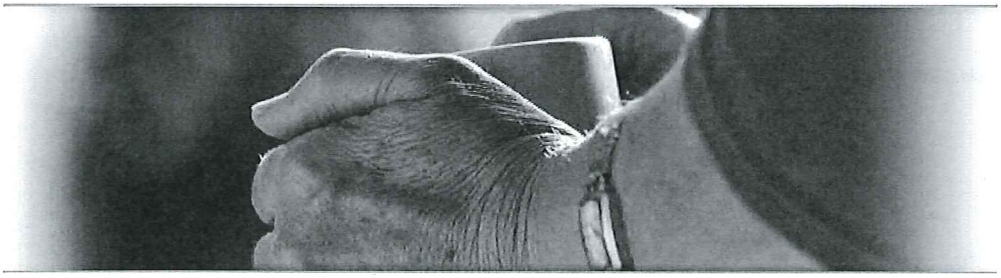
The hallmark pathology of MS is patchy demyelination, leading to nerve damage, which in most cases causes symptoms that adversely affect quality of life. Spasticity is one of the most common, chronic, and disabling of these symptoms, affecting up to 80% of MS patients over their lifetimes. Spasticity refers to an abnormal, involuntary tightness of muscles, which increases when the muscles are rapidly stretched, so that the associated joint appears to resist movement. Some of the features of spasticity include muscle stiffness, difficulty straightening joints, reduced mobility, limb weakness, shaking, intermittent spasms and pain. As a result of the increased muscle tone due to spasticity, "simple," everyday movements become difficult or impossible altogether. In addition, painful muscle spasms can lead to difficulty with sleeping, sitting in a chair or lying in bed. Occasionally, spasms may be triggered by fairly minor irritations such as tight clothing, a full bladder or bowel, urinary tract infection or skin irritation, such as from a pressure sore. Moderate to severe spasticity can lead to significant impairment.



There is no cure for spasticity, and it is widely recognized that currently available oral treatments afford only partial relief and have unpleasant side effects. Sativex offers the prospect of treating patients who have failed existing oral therapies and who might otherwise require invasive and costly alternative treatment options such as intrathecal baclofen or surgery.

There is a very clear need for new treatments for MS symptoms. According to the MS Society, "There are few effective treatments for the symptoms of MS. Most of the current drugs only benefit a minority of people and frequently have adverse side effects... this is especially true of pain control, where few treatments are effective... Available treatments for spasticity... afford partial relief and have unpleasant side effects."

For more information from the MS Society, **click here.**



Sativex® is approved and marketed in the UK and SpainEurope for the relief of spasticity in MS. as a treatment for symptom improvement in patients with moderate to severe MS spasticity who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy.

In support those approvals, Sativex has been shown to provide effective relief of spasticity symptoms, including reduced spasms, improved sleep and improved function, in patients for whom existing anti-spasticity treatments have failed. During the course of the development program for Sativex in MS spasticity, GW has conducted Phase 2 and Phase 3 double-blind, randomized, placebo-controlled trials involving 1,294 patients. These trials have all been published in peer-reviewed journals. In each trial, patients were permitted to remain on stable doses of their background oral anti-spasticity medication and spasticity was measured using a 0 to 10 NRS. This scale has been validated for use in spasticity clinical trials.

The largest and most recent of the Phase 3 trials, published by A. Novotna, et al. in the April 2011 issue of European Journal of Neurology, was a two-part trial and employed an enriched trial design. During the first four-week period, all patients received Sativex single-blind. This was followed by a 12-week, double-blind period in which patients who had achieved a pre-determined level of response at the end of the prior four week period were randomized to Sativex or placebo in a conventional parallel group design. We designed this trial to demonstrate the size of clinical benefit achieved from Sativex in patients who had previously shown a capacity to respond to treatment.

Each of the two principal cannabinoids within Sativex, THC and CBD, possess pharmacological properties that provide a rationale to support the efficacy of Sativex in MS spasticity. In animal models of MS, the CB1 receptor plays a key role in the modulation of spasticity and spasms. While CBD has little activity at cannabinoid receptors, it does have neuroprotective properties, which are most likely mediated by its ability to modulate intra-cellular calcium. The key pharmacology of CBD in MS likely relates to its role as an agonist at TRP channels, critical for maintaining calcium homeostasis and as an inhibitor of adenosine uptake, providing a non-cannabinoid receptor mechanism for its anti-inflammatory properties. In addition, CBD has an anxiolytic effect, is anti-psychotic and is believed to mitigate some of the undesirable side effects of THC.

GW believes that MS spasticity represents a significant market opportunity for the United States and intends to commence a required Phase 3 clinical trial of Sativex for MS spasticity in 2014 intended to lead to submission of an NDA to the FDA for this indication.

Sativex is approved in New Zealand and Canada for the treatment of spasticity due to Multiple Sclerosis and also approved and marketed in Canada for the relief of neuropathic pain in MS and cancer pain.

**Click here for details of Sativex clinical trials in MS**

References:

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