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# UNDERWRITING FOCUS



# Medical Marijuana for the Treatment of Multiple Sclerosis – Wonder Drug or Fashion Trend?

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"From Pariah to Prescription" was the title of a review that appeared some years ago on the possible medical use of marijuana.<sup>1</sup> What then seemed utopian and provocative has now become reality! A recently published comprehensive meta-analysis came to the conclusion that the muscle relaxant and analgesic effects of THC in cases of multiple sclerosis (MS) were well documented.<sup>2</sup>

#### Why was an ancient remedy banned?

Marijuana has been known as a painkiller for more than 4,000 years and belongs to a group of botanical drugs that, like coca and opium, are still used today. The plant was introduced into European medicine from India in 1842, in order to alleviate pain, muscle spasms and convulsions associated with tetanus, rheumatism and epilepsy.<sup>3</sup>

However, because of problems with quality control and political pressure in a world of growing substance abuse, marijuana was banned from modern Western pharmacopoeias in 1961, when the United Nations decided that it did not have any medical or scientific effect. No wonder – at that time, no one knew that the human body has its own endocannabinoid system with painkilling properties!

#### What is medical marijuana?

Marijuana is one of the most popular recreational drugs. It can be smoked, inhaled, mixed with food, or drunk as a tea. Worldwide, between 128 and 232 million people between the ages of 15 and 65 used marijuana and other cannabis products in 2013.<sup>4</sup>

Medical marijuana refers to the use of marijuana in medical therapy to help reduce symptoms in chronically ill patients. It has proved effective in the management of chronic pain, muscular cramps and spasticity in patients with multiple sclerosis, nerve or spinal cord damage or Tourette's. For cancer and AIDS patients, marijuana can reduce nausea and vomiting and stimulate appetite and weight gain. However, treatment with marijuana is not a cure, but rather a palliative treatment.

In recent years, many countries have legalised medical marijuana and introduced specific laws and programmes to allow patients with severe diseases to use cannabis products to relieve their symptoms. The Netherlands has the longest tradition of medical marijuana use. There, medicinal marijuana has been available on

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#### **About This Series**

Underwriting Focus provides information about general aspects and new tendencies in underwriting. It's published semiannually and focuses on medical and non-medical topics along with detailed case samples. The complete issue, which is a client-only publication, additionally contains a "look across the fence" at underwriting practices in other countries. prescription for more than 10 years. But more and more countries around the world have been legalising the medical use of marijuana, including 17 EU member states, most recently France, Romania and the Czech Republic.<sup>5</sup> In the United States, 23 states and Washington, D.C. (May 2015), have introduced laws to permit the medical use of marijuana.<sup>6</sup>

# Marijuana in the case of multiple sclerosis

In Europe multiple sclerosis (MS) is the most common neurological disorder leading to permanent disability in young adults. The precise cause of the disease is still unknown. In genetically predisposed individuals, an autoimmune response to components of the central nervous system is presumed to occur. Particularly since immunomodulatory treatments cannot prevent the chronic progress of the disability, a key concern in the long-term care of MS sufferers is to improve their quality of life by alleviating symptoms. Here, painful muscle spasms constitute a special challenge. A worthwhile option for treating these is the marijuana extract nabiximols (Sativex®).

#### Nabiximols – Composition

Nabiximols (Sativex<sup>®</sup>) is marketed as a mouth spray. The alcoholic tincture contains the marijuana plant's two most important cannabinoids, delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD), in a 1:1 ratio. Whereas THC has muscle relaxant and psychoactive effects, amongst others, CBD has no psychoactive properties (it is not therefore a narcotic like THC) but has analgesic, antispasmodic, neuroprotective and anxiolytic effects. This mixture has proved its worth, as CBD is able to weaken the psychoactive and addictive potential of THC.

Small, non-psychoactive doses of THC, in combination with opiates, should be sufficient to produce a synergistic pain-relieving effect. Opiates and cannabinoids go well together, particularly as they do not occupy the same receptors. Marijuana stops opiate-induced sickness and nausea and leads to an increased effect, thus allowing the dose of opiate to be reduced.

#### Nabiximols – Effectiveness

Nabiximols is licensed to improve symptoms in patients who have moderate to severe spasticity due to MS, who have not responded adequately to any other anti-spastic drug therapy and who have shown a clear clinical improvement in spasticity-associated symptoms during a therapeutic trial (usually of four weeks' duration). The patients' subjective impression is decisive here. In assessing effectiveness, it is also important to get the opinion of family members and carers.

The abovementioned meta-analysis confirmed the effectiveness of the spray. Nabiximols proved to be of benefit for MS-related spasticity and also improved the quality of sleep. Not all patients respond equally well to nabiximols.<sup>7</sup>

In addition to accompanying physiotherapy, in most cases muscle relaxants are initially used to treat spasticity. However, a side effect of these is muscular weakness, which can affect the ability to walk or stand in a similar way to spasticity. This side effect is seen less with nabiximols and other cannabinoids. Where the drug therapy recommended as initial treatment does not adequately improve spasticity, Sativex<sup>®</sup> can be used as an add-on therapy. The dose varies and must be worked out for each individual patient.

The guidelines of the American Academy of Neurology refer not only to the anti-spastic and analgesic properties

### **Underwriting Comment**

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Multiple Sclerosis (MS), whether confirmed or suspected, is a relatively familiar disclosure for underwriters in some markets. Assessment guidelines for confirmed cases typically use the current level of disability, the frequency of attacks and the amount of time following the diagnosis to steer a decision. The use of marijuana products in the treatment of people with MS may lead underwriters to consider whether the therapy should play a more prominent role in risk assessment.

This article is an excellent summary of the rationale for treating people who have MS with cannabinoids. Medical marijuana extracts do not come with the psychoactive effect of the illicit version. They are also well tolerated and do not affect life expectancy positively or negatively, meaning that their use should not influence a mortality decision. A person using marijuana as the plant product to alleviate their symptoms should however be treated as a smoker of marijuana or cannabis resin. It remains unusual for terms to be available for Critical Illness, Income Protection and disability covers, including waiver of premium, for people diagnosed with, or suspected as having, MS. An exclusion clause could be a solution in some cases.

of marijuana but also to the calming effect on an over-active bladder.<sup>8</sup> However, studies showed no evidence of THC reducing MS-related tremor and, unfortunately, the neuroprotective potential of marijuana often described in animal experiments could not be transferred to humans.<sup>9</sup>

#### **Contraindications and risks**

The probability of developing dependence is estimated to be low. All the same, nabiximols is a narcotic and is accordingly subject to prescription requirements. In patients suffering from substance abuse, the indications should be evaluated with particular care. Suicidal tendencies, pregnancy and the presence of psychiatric disorders are contraindications for nabiximols.

Cognitive impairment can occur and driving ability, especially immediately after administration and at the start of therapy, can be restricted. Patients must be informed of the possibility of the reduced ability to drive and of any impairment of their ability to work.

Although 62 different studies also looked into side effects, so far no work has been done on the possible long-term side effects of using nabiximols for more than a year. Overall, tolerance is estimated to be "good".

Because nabiximols is administered in the oral cavity, the pharmacokinetics are in fact more favourable, with more reliable absorption than in the case of oral preparations, such as THC tablets, oil or tincture. The absorption of THC is highest when inhaled. However, the incidence of side effects from smoking – which so far has not been legalised – is a clear argument against this route of administration. Smoked marijuana also risks increasing the cognitive impairment already caused by MS, as an MRI-based study was able to show.<sup>10</sup>

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involved in many research projects and publications on the subject of medical use of cannabis for MS patients.

#### Endnotes

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