

# Medicinal use of cannabis in Europe

*The fact that more countries legalize the medicinal use of cannabis should not become an argument for unfettered and uncontrolled use*

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The beneficial medicinal properties of cannabis, especially for pain relief, are widely recognized. Yet its main active ingredient, tetrahydrocannabinol (THC), is listed as a schedule-1 illicit drug in the United Nations' Single Convention on Narcotic Drugs. This status has hampered the medicinal use of marijuana, which has prompted patients and physicians to lobby governments to approve its use to treat chronic pain. This in turn has triggered an intense debate between governments, regulators and law enforcement on one side, and physicians and patients on the other side, about whether to legalize a drug, the production, possession and usage of which is still illegal in many countries.

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In recent years, a number of nations have introduced specific laws and programmes to allow patients to use cannabis preparations in various forms to relieve the symptoms of a range of severe, disabling diseases. As a result, cannabis has been used to effectively relieve chronic pain, muscular cramps and spasticity in patients with multiple sclerosis or spinal cord damage, as well as for patients affected by neurogenic pain caused by nerve damage and other causes [1]. Patients with terminal cancer and AIDS have also benefitted from the use of cannabis to alleviate nausea and vomiting, and to stimulate appetite and weight increase [2].

However, there is no unique list of pathologies that can be treated with cannabis-based drugs, since it is not a cure, but rather a palliative treatment. It is up to physicians to decide under which circumstances cannabis should be prescribed and which patients could benefit from the treatment.

In the USA, 23 states and the District of Columbia have already legalized marijuana for medicinal or recreational (only in Washington state, Colorado, Oregon and Alaska) use, and more States are poised to follow. Interestingly, these states are not in compliance with US federal law, which strictly prohibits the possession and use of cannabis. In Europe, the situation is different, as the member states are free to set their own national drug laws, although all of them are parties of the UN Single Convention. The country with longest experience of cannabis use—both medicinal and recreational—is the Netherlands, where physicians have been able to prescribe cannabis preparations for patients for more than 10 years. The Dutch government has authorized the company Bedrocan BV to supply cannabis products. It grows the plants according to Good Agricultural Practice, and without using pesticides, and manufactures various preparations, characterized by different compositions of the active cannabinoids tetrahydrocannabinol (THC) and cannabidiol (CBD), to be taken by vaporization or as herbal tea. Bedrocan BV also supplies the preparations exported by the Office for Medicinal Cannabis at the Dutch Ministry of Health, Welfare and Sport to other European countries and is, to date, the sole supplier of cannabis products to Germany, Finland, Italy and Norway.

Another cannabis-based pharmaceutical product, Sativex, is a mixture of THC and

cannabidiol at a standardized dosage, which ensures therapeutic efficacy and avoids side effects—mainly psychotic ones. Sativex is available as a mouth-spray in a number of countries, but the manufacturer, GW Pharmaceuticals, is based in England, where cannabis has not yet been legalized for medicinal use. Even though the National Health Service (NHS) provides access to Sativex in a limited number of areas, it is rarely prescribed by physicians. Despite the international reforms and efforts to legalize medical marijuana, the British government seems uninterested in softening its approach to either cannabis in general or its medicinal use in particular, but the debate is still open.

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In Germany, the Federal Institute for Drugs and Medical Devices has authorized the medicinal use of cannabis for special cases, which was strongly encouraged by the Federal Administrative Court in 2005. Currently, about 300 German patients with severe medical conditions are allowed to buy cannabis products at any pharmacy to relieve their pain. The issue of costs is highly relevant in Germany, however, as palliative cannabis treatment, which can amount to between €800 and €1,000 per month, is not covered by the health insurance system. The issue was solved in July last year,



when the Administrative Court of Cologne ruled that severely ill people who suffer from chronic pain can cultivate their own cannabis plants. The court's reasoning was based on economic arguments: patients without adequate insurance to cover the costs of imported cannabis products should nonetheless have access to treatment. The court also stressed that the requirements of the patients need to be assessed on a case-by-case basis.

In Italy, the therapeutic use of cannabis was authorized first in 2007. A 2014 legislation abolished the previously long bureaucratic process required to obtain a cannabis prescription, making cannabis freely available to patients with a prescription from primary care physicians. This was possible thanks to the adoption of a special law that governs the "mode of delivery of drugs and galenic preparations based on cannabinoids for therapeutic purposes" by regions in Sicily, after Abruzzo, Puglia, Tuscany, Liguria, Veneto, Lombardy and Piemonte. In this regard, the national Government decided not to hinder the distribution of cannabis, but did seek to secure patient rights and safety, reiterating that cannabis-based drugs should be prescribed only "when other available medications

have proven to be ineffective or inadequate to the therapeutic needs of the patient". Unlike in Germany, the costs will be covered by the Regional Health System through a hospital pharmacy or the patient's health insurance. To reduce import costs, the Italian Ministry of Health has started a pilot project to cultivate cannabis plants and manufacture the products directly in Italy at the Military Chemical-Pharmaceutical Factory.

Spain is lagging behind Italy and Germany in terms of legalizing medicinal cannabis use, though it has made more progress than the UK. The possession and use of cannabis is still illegal, but it has been decriminalized. As such, people can grow and use the plant for personal and medical use without fear of being prosecuted. Catalonia in particular is putting pressure on the Spanish government to legalize medical marijuana for use to treat pain and nausea resulting from cancer—or chemotherapy treatments against it—AIDS, and other diseases that cause chronic pain or appetite loss. Catalonia also seeks to put an end to Barcelona's increasingly popular "cannabis clubs", which started as non-profit cooperatives for people who wanted to use marijuana medicinally, but have become popular tourist spots that contribute to the sale of

black market of cannabis. By legally controlling the supply of medical marijuana, the regional government hopes the need for the clubs will vanish.

Medical marijuana has also been legalized in other EU member states, most recently in France, Romania and the Czech Republic. The use of Sativex has been approved in 17 European countries, 9 of which have already made it available. Although European laws have not gone as far as legalizing cannabis, as Colorado or Washington State have in the USA, what has been done has acknowledged that there are serious medicinal uses of cannabis and should go some way to stifling the black market cannabis trade.

As more countries in Europe and elsewhere legalize the medicinal use of cannabis, scientific evidence becomes imperative to inform appropriate regulation and prescription. There are certainly concerns about using cannabis in this way, especially in the USA, where the use of therapeutic herbal cannabis-based preparations—marijuana and hashish—has created a largely unregulated market and encouraged abuse. The establishment of an adequate monitoring system, as for instance in the Italian region of Abruzzo, would help to prevent inappropriate use,

verify proper dosage and application and register any problems and side effects. This is not just a matter of consumption, but of administration and dosage. Indeed, in the majority of the countries where the use of medical cannabis has been legalized, the free cultivation or consumption of cannabis through smoking or eating is still prohibited. Patients should use specific pharmaceutical formulations with defined content and ingredients based on an appropriate treatment plan drawn up by the medical practitioner.

The problem with smoking cannabis is that it does not deliver the drug in a reproducible or predictable dosage and does not provide any therapeutic benefit. In fact, the contrary is true: smoking cannabis is associated with a progressive loss of cognitive abilities and an increased predisposition to psychiatric illness, such as schizophrenia. There is sufficient evidence that marijuana abuse damages the brain—especially among adolescents, whose brains are still developing—and causes cognitive decline, poor attention and memory, and even decreases intelligence. Brain imaging studies have shown that regular cannabis use modifies brain structure, with massive structural abnormalities in the brain's grey matter density, volume and shape, particularly in the nucleus accumbens and amygdala [3].

Perhaps most pertinently to the medicinal use debate, recent studies have also highlighted the risk that the acceptance of medical cannabis could have a

dangerous impact on the way that adolescents perceive the risks of cannabis abuse [4]. It is therefore essential to clearly separate the medical use of cannabis as a drug delivered in a controlled dose from its recreational abuse through smoking. This would also send an educational message to the public that cannabis, like any therapeutic drug, can have serious side effects if it is not properly prescribed and administered.

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For researchers who have spent years studying the therapeutic efficacy of drugs based on cannabinoids and endocannabinoids in neoplastic, neurological, metabolic and inflammatory diseases, as we have, the new laws being introduced open the way for hugely increasing knowledge in this field [5]. However, the demonization of cannabinoids in several countries, and the public and regulatory perception that cannabis is merely an illicit drug, has created sufficient prejudice and suspicion to put in place unreasonably stringent drug protocols that hugely disadvantage patients who could benefit from cannabis-derived drugs. The

public acceptance of cannabis for medicinal should therefore be based and nurtured entirely on clinical evidence of its efficacy and safety, as well as its convenience for patients and National Health Systems or agencies.

### Conflict of interest

The authors declare that they have no conflict of interest.

### References

1. Koppel BS, Brust JC, Fife T, Bronstein J, Youssof S, Gronseth G, Gloss D (2014) Systematic review: efficacy and safety of medical marijuana in selected neurologic disorders: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology* 82: 1556–1563
2. Sharkey KA, Darmani NA, Parker LA (2014) Regulation of nausea and vomiting by cannabinoids and the endocannabinoid system. *Eur J Pharmacol* 722: 134–146
3. Gilman JM, Kuster JK, Lee S, Lee MJ, Kim BW, Makris N, van der Kouwe A, Blood AJ, Breiter HC (2014) Cannabis use is quantitatively associated with nucleus accumbens and amygdala abnormalities in young adult recreational users. *J Neurosci* 34: 5529–5538
4. Hill KP (2014) Medical marijuana: more questions than answers. *J Psychiatr Pract* 20: 389–391
5. Pisanti S, Picardi P, D'Alessandro A, Laezza C, Bifulco M (2014) The endocannabinoid signaling system in cancer. *Trends Pharmacol Sci* 34: 273–282