

Purpose

In 1996, California voters approved an initiative that exempted certain patients and their primary caregivers from criminal liability under state law for the possession and cultivation of cannabis. In 2003, the Legislature enacted additional standards relating to medical cannabis.¹ While this legislation established a list of approved medical conditions for which medical cannabis may be recommended, most listed conditions were left unsubstantiated by additional description, causing confusion when determining if medical cannabis is an appropriate therapeutic tool.

It is for the benefit of physicians and patients that these medical cannabis recommendation guidelines have been established to help ensure that the substance is being used for the appropriate purposes. This document addresses the medicinal use of cannabis, rather than its recreational use, as the medical indications for the use of cannabis are quite limited.

All ethical standards and best medical practices to which physicians adhere to when prescribing medications, including controlled substances, remain applicable to physicians recommending medical cannabis.

Governing California Statute

I. Proposition 215 - The Compassionate Use Act of 1996ⁱ

On November 5, 1996, the people of California passed Proposition 215, which decriminalized the cultivation and use of cannabis by seriously ill individuals upon a physician's recommendation (*Health & Safety Code §11362.5*). Proposition 215 was enacted to “ensure that seriously ill Californians have the right to obtain and use marijuana [cannabis] for medical purposes where that medical use is deemed appropriate and has been recommended by a physician who has determined that the person's health would benefit from the use of marijuana

[cannabis],” and to “ensure that patients and their primary caregivers who obtain and use marijuana [cannabis] for medical purposes upon the recommendation of a physician are not subject to criminal prosecution or sanction” (*Health & Safety Code §11362.5(b)(1)(A)-(B)*).

II. Senate Bill 420 - The Medical Marijuana Program Act (MMP)^{ii,iii}

On January 1, 2004, Senate Bill 420 (Vasconcellos) became law, thus enacting the Medical Marijuana Program Act (MMP) (*Health & Safety Code §§ 11362.7-11362.83*). The intent of the MMP was to clarify Proposition 215 by stipulating how patients who could not grow their own cannabis should obtain the substance. The MMP thus permits a primary caregiver to be paid a “reasonable compensation” for services provided to a qualified patient “to enable that person to use marijuana [cannabis].” It also states that a patient may cultivate up to six mature plants or possess up to half a pound of processed cannabis for medical purposes.

The MMP also required the California Department of Public Health to establish and maintain a program for the voluntary registration of qualified medical cannabis patients and their primary caregivers through a statewide identification card system. The voluntary registration program is administered through a patient's county of residence. To be eligible for a medical cannabis card a patient must apply through his or her county of residence and the medical records must contain written documentation by the attending physician that the patient has been diagnosed with a serious medical condition and that the medicinal use of cannabis is appropriate. A “serious medical condition” is defined to include:

1. Acquired immune deficiency syndrome (AIDS)
2. Anorexia
3. Arthritis

1. Refer to the Glossary of Terms definition of “marijuana” for a description of the use of terminology.

4. Cachexia
5. Cancer
6. Chronic pain
7. Glaucoma
8. Migraine
9. Persistent muscle spasms, including, but not limited to spasms associated with multiple sclerosis
10. Seizures, including, but not limited to seizures associated with epilepsy
11. Severe nausea
12. Any other chronic or persistent medical symptom that either:
 - a. Substantially limits the ability of the person to conduct one or more major life activities as defined in the Americans and Disabilities Act of 1990 (Public Law 101-336).
 - b. If not alleviated, may cause serious harm to the patient's safety or physical or mental health.

The above list of serious medical conditions is broad, and in most cases not supported by solid clinical research.

Implementation of the MMP Act provided an element of professional qualifications and provider deliberation by calling for the attending physician to fulfill the following:

1. Possess a license to practice medicine or osteopathy in California issued by the Medical Board of California or the Osteopathic Medical Board of California. This license must be in good standing.
2. Take responsibility for an aspect of the medical care, treatment, diagnosis, counseling, or referral of the applicant (patient).
3. Perform a medical examination of the applicant (patient).
4. As a result of the medical examination, document in the patient's medical record that the patient has a serious medical condition and that the medical use of marijuana [cannabis] is appropriate.

5. Have the patient sign an authorized medical release of information. The county program cannot process the patient's application without the appropriate authorization for release of medical information.
6. Provide to the patient copies of the medical records stating that he or she has been diagnosed with a serious medical condition and that the medical use of marijuana [cannabis] is appropriate.

Therapeutic Benefits

Medical cannabis may be effective for the treatment of pain, nausea, anorexia, and other conditions, but the literature on this subject is inadequate, dosage is not well standardized, and cannabis side effects may not be tolerated.^{iv}

At present, cannabinoids are thought to exhibit their greatest efficacy when implemented for the management of neuropathic pain.^v Neuropathic pain is a form of severe and often chronic pain resulting from nerve injury, disease, or toxicity. Existing pharmacologic treatments for neuropathic pain are not optimal. There is a significant population of patients who do not receive adequate relief from their pain through the use of pharmacologic treatments.

Other putative clinical benefits of cannabis have been discussed in the literature, prompting the call for scientific study. Most notable, a Consensus Conference sponsored by the National Institutes of Health^{vi} and a review panel convened by the Institute of Medicine^{vii} advocated that controlled studies be performed for analgesia, appetite stimulation and cachexia; nausea and vomiting following chemotherapy; neurological and movement disorders; and glaucoma.

In 2001, the American Medical Association (AMA) Council on Scientific Affairs advocated that the National Institutes of Health (NIH) implement administrative procedures to facilitate grant applications to conduct well-designed clinical research into the medical utility of cannabis.^{viii} In 2008, the American College of Physicians (ACP) urged "an evidence-based review of marijuana's [cannabis] status as a Schedule I controlled substance to determine whether it should be reclassified to a different schedule."^{ix} One year later (2009), the AMA's House of Delegates put forward a clear-cut message that marijuana's [cannabis] Schedule

I status was no longer appropriate and interfered with legitimate medical research.^x Most recently, the California Medical Association's House of Delegates adopted policy urging that marijuana's [cannabis] status as a federal Drug Enforcement Administration Status I controlled substance be reviewed with the goal of facilitating research (*HOD 102a-10*).

In 1999, Governor Gray Davis signed SB 847, which commissioned the University of California to fund research expanding our understanding of the therapeutic value of cannabis. The University of California Center for Medicinal Cannabis Research (CMCR) was organized to conduct clinical and pre-clinical studies of cannabinoids, including smoked cannabis. CMCR developed a close working relationship with state and federal agencies to gain regulatory approvals, established panels of nationally-recognized experts to rigorously review the merit of applications, and fund carefully designed studies. CMCR reported upon the results of a number of studies to the California legislature in 2010.^{xi} Among these, four studies involved the treatment of neuropathic pain; all four demonstrated a significant improvement in pain after cannabis administration. The results of another study investigating patients with multiple sclerosis found a significant improvement in both objective measures of spasticity and pain intensity in patients whose standard therapy had been inadequate.

Health Risks

Multiple health risks have a documented association with cannabis use.

Addiction: Addiction to cannabis may be characterized by escalating use, inability to cut back, craving, harmful consequences, and physical dependence. Epidemiologic data from a national comorbidity study indicate that about 9% of adult cannabis users become addicted and that this risk is substantially increased among individuals who begin using before age 18. Although of little consolation, among adults the incidence is low compared to alcohol use (15%), opioids (23%) or nicotine (32%).^{xii}

Short Term Cognitive Effects: Cannabis intoxication causes well-defined impairments in the following brain functions: Memory, sense of time, sensory perception, attention span, problem solving, verbal fluency, reaction time, and psychomotor control. The short term effects of cannabis

last approximately 1-4 hours, depending on potency of the cannabis, the route of administration, and the tolerance of the user. There are no reported cases of death resulting from cannabis overdose.^{xiii}

Long Term Cognitive Effects: The possible medicinal use of cannabinoids for chronic diseases emphasizes the need to understand the long term cognitive effects of these compounds. Results of a meta-analysis indicated that there might be decrements in the ability to learn and remember new information in chronic users, whereas other cognitive abilities were unaffected.^{xiv} The authors opined that, under the more limited conditions of exposure that would likely be seen in a medical setting, the benefits could outweigh problematic effects and the therapy might thereby prove to be acceptable.

Adolescents and Young Adults: The evidence suggests that cannabis can adversely affect adolescents who initiate use early and young adults who become regular users.^{xv} Compared to adults, adolescents and young adults may have greater vulnerability to the toxic effects of cannabis on the brain, especially when alcohol and cannabis are used together. In addition to increased risk of addiction, use of cannabis among adolescents is associated with poorer educational outcomes and occupational attainment.^{xvi} There is also the possibility that cannabis increases the risk of developing mental illness in this age group.^{xvii}

Psychiatric Conditions: Cannabis intoxication can cause transient mood, anxiety, and psychotic symptoms. The relationship between cannabis use and long term risk of psychiatric disorders is less well understood. Cannabis use has been weakly correlated with long term risk of mood disorders and anxiety disorders. The association between cannabis use and psychotic disorders is more robust. Cannabis can unmask symptoms among individuals who have pre-existing vulnerability (such as a family history) to schizophrenia.^{xviii} Additionally, there is some evidence that cannabis may be an independent risk factor for the development of psychotic disorders such as schizophrenia. Although the mechanism is unknown, repeated studies have shown that cannabis use is correlated with an increase in the risk of manifesting schizophrenia, an illness that affects approximately 1% of the global population.^{xix}

Obstructive Lung Disease: Given the increased risk of chronic obstructive pulmonary disease (COPD) in tobacco smokers, there is concern that a similar risk may exist among smokers of cannabis. Cannabis smoking by itself probably does not lead to COPD^{xx} but smoking both cannabis and tobacco is associated with a greater risk of COPD than smoking only tobacco.^{xxi}

Lung Cancer: The constituents of cannabis smoke are quantitatively analogous to those of tobacco smoke, with the exceptions of delta-9-tetrahydrocannabinol (THC) - found only in cannabis - and nicotine - found only in tobacco. Paradoxically, epidemiologic findings are inconsistent with the biological plausibility of cannabis being carcinogenic in aerodigestive tissue. Using over 1,000 incident cancer cases and over 1,000 cancer-free controls matched to cases on age, gender, and neighborhood, investigators at UCLA found no positive associations for malignancies after adjusting for several confounders (including cigarette smoking).^{xxii} They concluded that the association of pharyngeal and pulmonary cancers with cannabis, even long-term or heavy use, is “not strong and may be below practically detectable limits.”

Motor Vehicle Accidents: Epidemiological studies have been inconclusive regarding whether cannabis use causes an increased risk of accidents; in contrast, unanimity exists that alcohol use increases crash risk.^{xxiii} In tests using driving simulation, neurocognitive impairment varies in a dose-related fashion, and are more pronounced with highly automatic driving functions than with more complex tasks that require conscious control, whereas alcohol produces an opposite pattern of impairment.^{xxiv} Cannabis smokers tend to over estimate their impairment and compensate effectively while driving by utilizing a variety of behavioral strategies. During driving simulation, experimental subjects under the influence of cannabis drive slowly, leave a large distance between themselves and the car in front of their simulated car, and avoid changing lanes.

Reproductive Risks: The compounds found in cannabis readily cross the placenta, where the growing fetus absorbs them, and pass into breast milk, where the nursing infant ingests them. Cannabis affects many aspects of reproductive physiology in both men and women, though the long term consequences of these effects remain

unclear.^{xxv} Cannabis use during pregnancy and early development has been correlated with low birth weight as well as developmental delay and behavioral problems including addiction, although the causal link to cannabis use has not yet been established.^{xxvi, xxix}

Physicians and Dispensaries

Investigative journalists have described lucrative clinics with salaried physicians who specialize in providing medical cannabis recommendations, potentially for undocumented medical conditions.^{xxvi, xxvii} Licensed physicians who already have or who are considering entering into a professional employment agreement with a cannabis clinic or dispensary for the purpose of evaluating patients and recommending cannabis should exercise caution to prevent violations of California’s bar on the corporate practice of medicine.

As a general rule, in most cases it is not appropriate for a physician to be hired by a non-physician. California has a strong long-standing public policy against permitting lay persons to practice any of the medical arts or to exercise control over the decisions made by healing arts practitioners. Physicians who are considering employment by a cannabis clinic or dispensary should confirm that *the business is a physician-owned medical practice or a professional medical corporation with physicians being the majority shareholder*. A cannabis clinic or dispensary that is not a *physician-owned medical practice or a professional medical corporation* may not *employ* physicians to provide medical services, such as diagnosing patients and recommending cannabis.

Physicians are strongly encouraged to seek professional legal advice before engaging in any business endeavor that involves the practice of medicine.

Preventing Cannabis Diversion for Non-Medical Use

The California cannabis harvest is very profitable and worth an estimated \$17 billion or more, dwarfing any other sector of California’s agricultural economy.^{xxx} Although the scope of diversion of this crop is not known, California’s approach to medical cannabis has in some cases, virtually decriminalized recreational use and has led to excesses. As a result of lax regulation, the number of medical cannabis

dispensaries has exploded. Before local law enforcement curtailed activity, there were estimates of 800 to 900 storefront shops selling cannabis in Los Angeles alone. It is a rational assumption that, unless physicians adhere to their ethical and fiduciary responsibilities to patients, controlling the number of dispensaries or limiting the number of plants cultivated will not suffice in the challenge to prevent the diversion of cannabis for recreational use.^{xxx}

Prescribing controlled substances normally brings with it a risk of regulatory oversight, thus the regulatory vacuum that currently exists in most states permitting the use of medical cannabis needs to be corrected. In essence, states that have adopted medical cannabis laws should establish a mechanism to allow their boards of medicine to thoroughly supervise the recommendations made by physicians for medical cannabis.^{xxxi} It is this regulatory rationale that prompted California's attorney general, Jerry Brown, to issue "Guidelines for the Security and Non-Diversion of Marijuana [Cannabis] Grown for Medical Use," in 2008.^{xxxii} These guidelines were intended to verify the existence of a bona fide doctor/patient relationship when cannabis is recommended for therapy or palliation.

Disciplinary Consequences

I. California Law

State law prohibits disciplining a physician for recommending cannabis for treatment of a serious medical condition (*Health & Safety Code §11362.5(c)*). However, the Medical Board of California can and does take disciplinary action against physicians who fail to comply with accepted medical standards when recommending cannabis. In a May 13, 2004 press release, the Medical Board of California clarified that these accepted standards are the same ones that a reasonable and prudent physician would follow when recommending or approving any medication.^{xxxiv} These standards include the following:

1. History and good faith examination of the patient.
2. Development of a treatment plan with objectives.
3. Provision of informed consent including discussion of side effects.
4. Periodic review of the treatment's efficacy.

5. Consultation, as necessary.

6. Proper record keeping that supports the decision to recommend the use of medical marijuana [cannabis].

II. Federal Law

The federal government regulates marijuana [cannabis] through the Controlled Substances Act (*21 U.S.C. §811*). It is important to note that this Act does not recognize a difference between the recreational and medicinal use of marijuana [cannabis].

Under federal law, marijuana [cannabis] is currently classified in statute as a Schedule I drug, meaning it has no generally recognized medical use. On June 6, 2005, the United States Supreme Court ruled that the federal Controlled Substances Act is valid even as applied to intrastate, noncommercial cultivation, possession and use of marijuana [cannabis] for personal medical use on the advice of a physician.^{xxxv} The Court's ruling maintains the existing federal prohibition against possession, cultivation, and distribution of marijuana [cannabis]. The ruling has no direct impact on California's current law (CUA and MMP), nor does it narrow or otherwise negatively affect the Ninth Circuit's ruling in *Conant v. Walters*, which stated that physicians have a First Amendment right to discuss treatment options with their patients, including treatment with medical marijuana [cannabis].

Federal law establishes a clear prohibition against knowingly or intentionally distributing, dispensing, or possessing marijuana [cannabis] (*21 U.S.C. §841-44*). A person who aids and abets another in violating federal law, 18 U.S.C. §2, or engages in a conspiracy to purchase, cultivate, or possess marijuana [cannabis], 21 U.S.C. §846, can be punished to the same extent as the individual who actually commits the crime. The penalty for a first-time violation of these provisions in the case of less than 50 kilograms of marijuana [cannabis] is imprisonment for a term of up to five years, a fine of up to \$250,000, or both. The penalty for a violation committed after a prior drug conviction is imprisonment for a term of up to ten years, a fine of \$500,000, or both (*21 U.S.C. §841(b)(1)(D)*).

Other federal sanctions are also possible. If a physician were to aid and abet or conspire in a violation of federal law,

the federal government might revoke the physician's DEA registration through an administrative procedure. Physicians should also be aware that a felony conviction relating to the unlawful manufacture, distribution, prescription, or dispensing of a controlled substance results in mandatory exclusion from the Medicare and Medi-Cal programs (42 U.S.C. §1320a-7(a)(4)).

For more information, refer to CMA medical-legal document #1315, "The Compassionate Use Act of 1996: The Medical Marijuana Initiative."

Best Practices for Physicians

The enactment of Proposition 215 through its overwhelming support by the people of California embodied the belief that patients were being denied a medication that could alleviate suffering. Nowhere is this more readily evident than for the treatment of certain conditions (pain, nausea and vomiting secondary to chemotherapy, spasticity, and anorexia associated with AIDS). The efficacy of medical cannabis in other medical illnesses is less well-defined and will require additional time for elucidation through scientific inquiry.

Oral forms of THC, available by prescription in the United States for nausea and vomiting associated with cancer chemotherapy, include dronabinol (Marinol) and nabilone (Cesamet). These cannabinoids are less effective with severely emetogenic drugs such as cisplatin, while other drugs such as ondansetron (Zofran and others) and aprepitant (Emend) appear to be more effective and better tolerated.^{xxxvi} Dronabinol is also approved for the treatment of anorexia associated with AIDS. Another cannabinoid, nabiximols (Sativex – GW Pharmaceuticals), is a liquid extract containing THC and cannabidiol, another constituent of botanical cannabis.^{xxxvii} Approved in Canada for adjunctive treatment of central neuropathic pain in multiple sclerosis, it is in phase III trials in the US for treatment of intractable cancer pain.

Over a decade ago, some NIH Conference^{xxxviii} and Institute of Medicine^{xxxix} participants stressed that, because the whole cannabis plant contains many possibly active cannabinoids besides THC, its possible efficacy may not be replicated by medications containing only THC. Consideration of smoked or preferable vaporized cannabis should be considered if

oral medications are not effective or if the doctor/patient jointly decide to exclude the use of these medications for a valid reason (i.e., cost).

Patients should be advised to keep medical cannabis in a secure location so as to avoid diversion particularly to children and/or adolescents. They should be advised to consume as little as possible to produce the desired medical effect. Patients should be queried as to the development of tolerance and withdrawal phenomena and their ability to control the intake of medical cannabis. In addition, testing for illicit drugs through toxicology analysis should be considered, as clinically indicated, to ensure that illicit drugs are not being consumed. The physician should inquire as to the outcome of the use of this medication in terms of its efficacy and side effects on a periodic basis. Patients should be reminded not to drive or operate heavy machinery while under the influence of cannabis.

The physician should assess and document patient-specific risks, benefits, and alternatives to treatment with cannabis. The physician should take particular precaution among at-risk populations, including children and young adults, pregnant or breast feeding women, and individuals with mental illness, and those with pre-existing histories of addiction. The physician should also have the capacity to screen and either treat or refer patients who develop adverse effects such as addiction.

Additionally, physicians will have to keep abreast of emerging literature on the subject of medical cannabis. It is hoped that "neither popular votes nor congressional 'findings' should be permitted to trump scientific evidence in deciding whether or not cannabis is an appropriate pharmaceutical agent to use in modern medical practice."^{xl, xli} By maintaining interest and valuing their fiduciary responsibilities, physicians can potentially improve the lives of the patients they serve using medical cannabis as they do with other pharmaceuticals.

Conclusions

Medical cannabis may be effective for treatment of nausea, anorexia, pain and other conditions (i.e., spasticity), but more clinical research is needed to update practitioners regarding specific indications, dosing, and the management of side effects. Legislative decision-making is a poor

alternative to scientific analysis in deciding whether or not cannabis is an appropriate pharmaceutical agent. Additional basic scientific and clinical research is needed to evaluate cannabinoids as medical agents. Regulation of dispensaries and physicians who recommend medical cannabis remains a long-term goal to prevent the use of cannabis for virtually any and all complaints. The professional ethic of health care providers should be implemented through regulatory oversight to optimize patient safety and wellbeing and, potentially, to prevent diversion of medical cannabis to recreational users.

Glossary of Terms

Cannabinoids

The term “cannabinoid” has different meanings. In a more narrow sense, it designates the natural phytocannabinoids found in the cannabis plant, as well as their synthetic versions and derivatives. In the broadest sense, it denotes all molecules that bind to the cannabinoid receptors, including the endogenous cannabinoids (endocannabinoids).

Cannabinoid Receptors

Several cells in the brain and other organs contain specific protein receptors that recognize THC and some other cannabinoids and trigger cell responses. Other cannabinoids do not bind to these cannabinoid receptors and exert their effects by other ways. The discovery of specific cannabinoid receptors prompted the search for putative naturally-occurring chemicals that interact with the receptors, the endocannabinoids. There are at least two cannabinoid receptor types, CB1 receptors, and CB2 receptors. CB1 receptors are found in high concentrations within the brain and spinal cord. They are also present in certain peripheral cells and tissues (some neurons, some endocrine glands, leukocytes, spleen, heart and parts of the reproductive, urinary and gastrointestinal tracts). CB2 receptors are expressed primarily by immune cells and tissues (leukocytes, spleen and tonsils).

Cannabis

Cannabis sativa L. is the botanical name and Latin binomial of hemp. There are 483 known identifiable chemical constituents present in the cannabis plant. The most distinctive and specific class of compounds are the

cannabinoids (66 known), which are produced only by the cannabis plant. Because the potency and content of cannabis varies significantly, depending on its strain and the conditions of cultivation, harvesting, and storage/processing, “cannabis” is not a homogenous substance, unlike other medical products. It can also be contaminated with pesticides, heavy metals, and harmful microbes. Current methods of administration do not assure a reliable and reproducible dose.

Cannabis-derived products

These are products containing cannabis or cannabis extracts. The term may refer to standardized prescription medications, such as nabiximols (see below), or to products sold by cannabis dispensaries or prepared by individual consumers.

Dispensaries

These are cannabis distribution centers that sell different varieties of herbal cannabis, cannabis-derived products, and cannabis consumption devices. Dispensaries may cultivate their own cannabis, but generally purchase the cannabis from external vendors.

Dronabinol

Dronabinol is another name for the naturally occurring (-)-trans-isomer of delta-9-THC, often used in a medical context in the scientific literature. Dronabinol is often used to refer to the synthetically manufactured molecule. There is no chemical or pharmacological difference between the natural dronabinol found in the plant and dronabinol that is manufactured synthetically or semi-synthetically.

Endocannabinoids

The endogenous ligands of the cannabinoid receptors have been termed endogenous cannabinoids or endocannabinoids. Endocannabinoids are produced by both humans and animals. Some endocannabinoids are arachidonyl-ethanolamide (anandamide), 2-arachidonyl glycerol (2-AG), 2-arachidonylglycerol ether (noladin ether), arachidonyl-ethanolamine (virodhamine), and N-arachidonyl-dopamine (NADA).

Hemp

Depending on THC and other cannabinoid content, hemp can be divided into fiber types and drug types. In the US and Canada, the term “hemp” is usually applied only to fiber

hemp, in contrast to the terms “marijuana” or “cannabis,” which generally apply to drug types (1-20+% THC). (Grotenhermen and Russo, 2002).

Herbal (or botanical) cannabis

This term refers to the leaves or flowers of the cannabis plant, as distinguished from cannabis-derived products.

Marijuana

Marijuana is a slang term for the dried leaves and flowers of the varieties of the cannabis plant that are rich (1-20+% THC). Throughout these guidelines, the scientific term “cannabis” will be used, except where the term “marijuana” is contained in a direct quotation.

Marinol®

Marinol® is a preparation of synthetic dronabinol, dissolved in sesame oil, as capsules of 2.5, 5, and 10 mg dronabinol. Marinol® is available in the US, Canada, and some European countries. Generic versions of Marinol® are now available.

Medicinal cannabis

This refers to cannabis that is recommended by a physician to be used by a patient for medical purposes.

Nabilone

Nabilone is a synthetic derivative of delta-9-THC with a slightly modified molecular structure, available in some countries on prescription. Nabilone is sold under the trademarked name of Cesamet®.

Nabiximols

Nabiximols is the United States Adopted Name (USAN) applied to Sativex®, a cannabis-derived prescription medication. Sativex® is approved in the UK, Spain, Germany, New Zealand, and Canada as an adjunctive

treatment for spasticity in patients with multiple sclerosis (MS). It is also provisionally approved in Canada as an adjunctive treatment for neuropathic pain in MS and for persistent background pain associated with advanced cancer. Sativex® is comprised of a defined ratio (1:1) of THC and CBD (cannabidiol—a nonpsychoactive cannabinoid), as well as other minor cannabinoids and active plant components. It is administered as an oromucosal spray absorbed by the lining of the mouth.

Primary caregivers

Under California law, the term “primary caregiver” refers to the individual, designated by a qualified patient (i.e., one with a physician’s recommendation to use cannabis for medical purposes), who has consistently assumed responsibility for the patient’s housing, health, or safety. The California Supreme Court ruled that a person whose “caregiving” consists principally of supplying cannabis and instructing on its use, and who otherwise only sporadically takes some patients to medical appointments, cannot qualify as a “primary caregiver” under the CUA. (*People v. Mentch* (2008) 45 Cal.4th 274, 85 Cal.Rptr.3d 480.) The court concluded that a primary caregiver must prove at a minimum that he/she 1) consistently provided caregiving, 2) independent of any assistance in taking medicinal cannabis, 3) at or before the time he/she assumed responsibility for assisting with medicinal cannabis. A primary caregiver must be the principal, lead, or central person responsible for rendering assistance in the provision of daily life necessities. Therefore, a dispensary generally will not qualify as a primary caregiver.

THC

THC or delta-9-tetrahydrocannabinol is the primary psychoactive cannabinoid found in the cannabis plant. ■

- ⁱ Brown E. Guidelines for the Security and Non-Diversion of Marijuana Grown for Medical Use. In: Attorney General DoJ, State of California, ed; Aug 2008. Last Accessed March 9, 2011: <http://ag.ca.gov/cms_attachments/press/pdfs/n1601_medicalmarijuanaguidelines.pdf>.
- ⁱⁱ SB 420 (Vasconcellos, 2003) Last Accessed March 9, 2011: <http://leginfo.ca.gov/pub/03-04/bill/sen/sb_0401-0450/sb_420_bill_20031012_chaptered.pdf>.
- ⁱⁱⁱ “Physician Responsibilities.” California Department of Public Health. 2010. Last Accessed March 9, 2011: <<http://www.cdph.ca.gov/programs/Pages/MMPDrRespon.aspx>>.
- ^{iv} Medical Marijuana. The Medical Letter® On Drugs and Therapeutics. January 25, 2010;52(1330).
- ^v Rahn EJ, Hohmann AG. Cannabinoids as pharmacotherapies for neuropathic pain: from the bench to the bedside. *Neurotherapeutics*. Oct 2009;6(4):713-737.
- ^{vi} Workshop on the Medical Use of Marijuana. Paper presented at: Report to the Director, National Institutes of Health, by the Ad Hoc Group of Experts, 1997; Bethesda, MD. <<http://www.nih.gov/news/medmarijuana/MedicalMarijuana.htm>> Archived offline; for retrieval, please send a detailed request to olib@od.nih.gov. Last Accessed March 9, 2011.
- ^{vii} Marijuana and Medicine: Assessing the Science Base, 1999. Last Accessed March 9, 2011: <http://www.nap.edu/openbook.php?record_id=6376>.
- ^{viii} Report 3 of the Council on Science and Public Health (I-09) Use of Cannabis for Medicinal Purposes (Resolutions 910, I-08; 921, I-08; and 229, A-09). Last Accessed March 9, 2011: <<http://www.ama-assn.org/ama/no-index/about-ama/13625.shtml>>.
- ^{ix} Taylor T. American College of Physicians Supporting Research into the Therapeutic Role of Marijuana: A Position Paper: (Available from American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106.); 2008. Last Accessed March 9, 2011: <http://www.acponline.org/advocacy/where_we_stand/other_issues/medmarijuana.pdf>.
- ^x O’Reilly K. AMA Meeting Delegates Support Review of Marijuana’s Schedule I Status. *AmedNews.com*; November 23, 2009. Last Accessed March 9, 2011: <<http://www.ama-assn.org/amednews/2009/11/23/prse1123.htm>>.
- ^{xi} Grant I, Atkinson J, Mattison A, Coates T. Center for Medicinal Cannabis Research. Report to the Legislature and Governor of the State of California presenting findings pursuant to SB847 which created the CMCR and provided state funding: UC San Diego; February 10, 2010. Last Accessed March 9, 2011: <http://www.cmcr.ucsd.edu/images/pdfs/CMCR_REPORT_FEB17.pdf>.
- ^{xii} Anthony J, Warner L, Kessler R. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances and inhalants: basic findings from the National Comorbidity Study. *Clin Exp Psychopharmacol*. 1994;2:244-268.
- ^{xiii} Welch S, Martin B. The pharmacology of marijuana. In: Graham A, Schultz T, Mayo-Smith M, Ries R, Wilford B, eds. *Principles of Addiction Medicine* 3rd ed. Chevy Chase, MD: American Society of Addiction Medicine; 2003:249-270.
- ^{xiv} Grant I, Gonzalez R, Carey CL, Natarajan L, Wolfson T. Non-acute (residual) neurocognitive effects of cannabis use: a meta-analytic study. *J Int Neuropsychol Soc*. Jul 2003;9(5):679-689.
- ^{xv} Hall W. The adverse health effects of cannabis use: what are they, and what are their implications for policy? *Int J Drug Policy*. Nov 2009;20(6):458-466.
- ^{xvi} Ibid.
- ^{xvii} D’Souza DC. Cannabinoids and psychosis. *Int Rev Neurobiol*. 2007;78:289-326.
- ^{xviii} Arseneault, Cannon et al. “Causal association between cannabis and psychosis: Examination of the evidence.” *British Journal of Psychiatry*. No. 184, 2004: 110-117.
- ^{xix} Moore, Zammit et al. 2007.
- ^{xx} Tashkin DP. Does smoking marijuana increase the risk of chronic obstructive pulmonary disease? *Cmaj*. Apr 14 2009;180(8):797-798.
- ^{xxi} Tan WC, Lo C, Jong A, et al. Marijuana and chronic obstructive lung disease: a population-based study. *Cmaj*. Apr 14 2009;180(8):814-820.

- ^{xxii} Hashibe M, Morgenstern H, Cui Y, et al. Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study. *Cancer Epidemiol Biomarkers Prev.* Oct 2006;15(10):1829-1834.
- ^{xxiii} Sewell RA, Poling J, Sofuoglu M. The effect of cannabis compared with alcohol on driving. *Am J Addict.* May-Jun 2009;18(3):185-193.
- ^{xxiv} Ibid.
- ^{xxv} Schuel, H. "Tuning the oviduct to the anandamide tone." *J Clin Invest* 116(8): 2087-90, 2006.
- ^{xxvi} Fergusson, D. M., L. J. Horwood, et al. 2002.
- ^{xxvii} *BJOG* 109(1): 21-7.
- ^{xxviii} Samuels, D. "Dr. Kush: How medical marijuana is transforming the pot industry." *The New Yorker, A Reporter at Large.* July 28, 2008. Last Accessed March 9, 2011: <http://www.newyorker.com/reporting/2008/07/28/080728fa_fact_samuels#ixzz1FrjpERxr>
- ^{xxix} Wohlsen, M. Leff L. "'Medical' Marijuana Becomes A Major Economic Force in California." *CNSNEWS.com.* Last Accessed March 9, 2011: <<http://cnsnews.com/node/51263>>.
- ^{xxx} Ibid.
- ^{xxxi} Cohen, P.J. "Medical marijuana 2010: It's time to fix the regulatory vacuum." *Journal of Law and Medical Ethics.* September 2010, 38(3): 654-666.
- ^{xxxii} Ibid.
- ^{xxxiii} Brown E. Guidelines for the Security and Non-Diversion of Marijuana Grown for Medical Use. In: Attorney General DoJ, State of California, ed; Aug 2008. Last Accessed March 9, 2011: <http://ag.ca.gov/cms_attachments/press/pdfs/n1601_medicalmarijuanaguidelines.pdf>.
- ^{xxxiv} "Medical Marijuana." The Medical Board of California, Department of Consumer Affairs. May 7, 2004. Last Accessed March 9, 2011: <http://www.mbc.ca.gov/medical_marijuana.html>.
- ^{xxxv} *Gonzalez v. Raich* (2005) 525 U.S. 1, 162 L.Ed.2d 1, 125 S.Ct. 2195.
- ^{xxxvi} Medical Marijuana. *The Medical Letter® On Drugs and Therapeutics.* January 25, 2010;52(1330).
- ^{xxxvii} Ibid.
- ^{xxxviii} Workshop on the Medical Use of Marijuana. Paper presented at: Report to the Director, National Institutes of Health, by the Ad Hoc Group of Experts, 1997; Bethesda, MD.
- ^{xxxix} *Marijuana and Medicine: Assessing the Science Base*, 1999. Last Accessed March 9, 2011: <http://www.nap.edu/openbook.php?record_id=6376>.
- ^{xl} Cohen PJ. Medical marijuana: the conflict between scientific evidence and political ideology. Part one of two. *J Pain Palliat Care Pharmacother.* 2009;23(1):4-25.
- ^{xli} Ibid.