American Society of Health-System Pharmacists®

ASHP Policy Analysis

Medical Marijuana

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As more states allow for the medical use of marijuana, health-system pharmacists may increasingly encounter patients taking it to ease their chronic pain, disease- or treatment-related anorexia, or other symptoms. New Jersey is considering requiring hospitals to distribute marijuana to patients with prescriptions.[1] This paper will discuss the medical use of marijuana and synthetic cannabinoids and the complicated landscape pharmacists must navigate regarding the use of these agents.

Medical marijuana is the use of botanical marijuana to alleviate the symptoms of and treatment for certain diseases, such as cancer, HIV/AIDS, multiple sclerosis, and glaucoma. The active ingredients in marijuana are tetrahydrocannabinol (THC) and other cannabinoids.[2] "Conditions for which marijuana is commonly recommended include nausea caused by cancer chemotherapy; anorexia or wasting due to cancer, AIDS, or other diseases; chronic pain; spasticity caused by multiple sclerosis or other neurologic disorders; and glaucoma."[3]

A reason for marijuana's popularity is that it takes effect quickly, whereas synthetic cannabinoids take longer for their effects to be felt. When inhaled, marijuana takes effect in approximately 5 minutes when used for stomach pain, nausea, and vomiting and takes effect in approximately 10 to 15 minutes when used to improve appetite.[4] Marijuana that is ingested rather than inhaled takes between 30 minutes and 1 hour to take effect.[4]

Dronabinol is the FDA-approved drug therapy for tetrahydrocannabinol (THC).[5] Dronabinol takes approximately half an hour to 1 hour to take effect and its peak effect lasts from 2 to 4 hours.[5] "Duration of action for psychoactive effects is 4 to 6 hours, but the appetite stimulant effect of dronabinol may continue for 24 hours or longer after administration."[6] Marinol is FDA-approved to treat cancer chemotherapy patients' nausea and vomiting and AIDS patients' appetite loss.[7] A study of patients taking opioids for chronic pain found that patients who also took dronabinol reported significant pain relief and were more satisfied with their treatment.[8] However, medical marijuana advocates do not find dronabinol to be a comparable substitute because the marijuana plant "contains more than 400 known chemical compounds, including about 60 active cannabinoids in addition to THC."[9] Advocates argue that scientists do not know which cannabinoids "provide which therapeutic effects."[9]

Complicating marijuana's medical use is that it is categorized as a Schedule I controlled substance under the Controlled Substances Act (CSA).[10] Schedule I is the most restrictive category and is reserved for a drug or substance that has a high potential for abuse, does not have an accepted medical use in the United States, and for which there is a lack of accepted safety for use.[10] "The CSA does not distinguish between the medical and recreational use of marijuana."[9] A drug must meet five conditions to meet the definition of an accepted medical use as described in **Exhibit 1**.[11]

Exhibit 1

A drug has an accepted medical use if it meets the following conditions.[11]

1. The drug's chemistry is known and reproducible.
2. There are adequate safety studies.
3. There are adequate and well-controlled studies proving efficacy.
4. The drug is accepted by qualified experts.
5. The scientific evidence is widely available.

The Food and Drug Administration (FDA), the Drug Enforcement Administration (DEA), and the Office of National Drug Control Policy (ONDCP) do not support patients' smoking marijuana for medical purposes.[12]

However, some argue that medical marijuana should be regulated by the FDA since medical marijuana is used as a drug and, as such, should be evaluated by the FDA as an investigational drug.[13]

Studying Medical Marijuana

The Institute of Medicine (IOM) reports that data on cannabinoid use are "moderately promising" for treating muscle spasticity and "least promising" for movement disorders, epilepsy, and glaucoma.[5] "The therapeutic effects for cannabinoids are most well-established for THC, which is the primary psychoactive ingredient of marijuana. But it does not follow from this that smoking marijuana is good medicine."[5]

IOM suggests that "marijuana should rarely be recommended unless all reasonable options have been eliminated."[5]

IOM recommends continuing research into "synthetic and plant-derived cannabinoids" with a focus on "developing rapid-onset, reliable, and safe delivery systems."[5] Clinical trials also should focus on cannabinoids' psychological effects.[5] IOM further recommends studies on the health risks of smoking marijuana.[5] Specifically, IOM suggests medical marijuana clinical trials be conducted in the following manner.

> "Short-term use of smoked marijuana (less than six months) for patients with debilitating symptoms (such as intractable pain or vomiting) must meet the following conditions:
>
> - failure of all approved medications to provide relief has been documented,
> - the symptoms can reasonably be expected to be relieved by rapid-onset cannabinoid drugs,
> - such treatment is administered under medical supervision in a manner that allows for assessment of treatment effectiveness, and
> - involves an oversight strategy comparable to an institutional review board process that could provide guidance within 24 hours of a submission by a physician to provide marijuana to a patient for a specified use."[5]

Studies have shown that synthetic cannabinoids are effective but that patients using them experience an increase in nonserious adverse events. A quantitative systematic review of cannabinoids used to treat nausea and vomiting caused by chemotherapy found that synthetic cannabinoids were slightly more effective than conventional antiemetics.[14] Patients also preferred the synthetic cannabinoids, but side effects were more prevalent.[14] Side effects included a sensation of a "high," euphoria, drowsiness, hallucinations, paranoia, and a decrease in blood pressure.[14] The three synthetic cannabinoids tested were oral nabilone, oral dronabinol, and intramuscular levonantradol.[14]

In a systematic review of 31 medical cannabis studies, 23 randomized control trials and 8 observational studies, showed an increase in nonserious adverse events among patients using cannabinoids.[15] The most common nonserious adverse event patients reported was dizziness.[15] In the randomized controlled trials, there were 4779 adverse events reported and 96.6% of those events were not serious.[15] Serious adverse events included a multiple sclerosis relapse, vomiting, and urinary tract infection.[15]

Marijuana authorized for research is available from the University of Mississippi under a contract with the National Institute on Drug Abuse.[9] However, "the marijuana is difficult to obtain even by scientists whose research protocols have been approved by the FDA."[9]

Practitioners investigating the effectiveness of marijuana must be registered to conduct research using a Schedule I controlled substance that includes a determination of the practitioner's competency and the research protocol's merits.[16] The Attorney General can deny an initially approved application on specific grounds such as if the applicant's license or registration to practice was suspended, revoked, or denied by a competent state authority or recommended for suspension, revocation, or denial.[16] Research with controlled substances on all other schedules requires the Attorney General to register a practitioner "if the applicant is authorized to dispense, or conduct research with respect to, controlled substances under the laws of the State in which he practices."[16] Registration to conduct research using a Schedule I controlled substance can be denied if the Attorney General determines that the research would be inconsistent with the public interest.[16] Factors that would be considered to determine the public interest include a state board's recommendation and the applicant's experience with controlled substances.[16]

State Actions

A growing number of states are allowing the medical use of marijuana and more states are considering going that direction as well. Fifteen states and the District of Columbia have approved marijuana for medical use: Alaska, Arizona, California, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, and Washington.[17] New Jersey's medical marijuana program will start in January 2011 after the state legislature approved a bill delaying its implementation that was requested by Governor Chris Christie.[18] The program was originally scheduled to begin October 1, 2010.[1] "Christie has suggested having the marijuana grown at Rutgers University and distributed by hospitals."[1] However, Rutgers University declined the governor's request to grow marijuana because doing so could put the university's federal funding at risk.[19]

Nine states have pending legislation to legalize medical marijuana as of February 3, 2011: Connecticut, Delaware, Idaho, Illinois, Maryland, Mississippi, New Hampshire, New York, and Oklahoma.[20]

While some states have enacted laws making marijuana use legal if prescribed by an authorized prescriber, these laws do not counteract federal law prohibiting its use and do not protect patients, caregivers, and providers from prosecution under the CSA.[9]

State-Federal Tension

This tension between state and federal laws has been fueled by several major court cases. In 2001, the DEA denied a citizens' petition to reschedule marijuana from a Schedule I CSA that was submitted in 1995.[9] In Conant v. Walters (2002), the federal district court in California issued a preliminary injunction in April 1997 prohibiting "federal officials from threatening or punishing physicians for recommending marijuana to patients suffering from HIV/AIDS, cancer, glaucoma, or seizures or muscle spasms associated with a chronic, debilitating condition."[9] The injunction was made permanent, the Ninth Circuit Court upheld the district court's permanent injunction order, and the U.S. Supreme Court refused to hear the case.[9]

In Gonzales v. Raich (2005), the U.S. Supreme Court reached a 6-3 decision that allows the DEA to continue enforcing the "CSA against medical marijuana patients and their caregivers, even in states with medical marijuana programs."[9] This ruling does not invalidate state medical marijuana laws.[9]

However, a 2009 DOJ memorandum to U.S. Attorneys stated that federal resources should not be used to prosecute persons whose actions comply with state laws permitting medical use of marijuana.[9] Previously, DEA agents raided medical marijuana dispensaries in California.[9]

A more permanent change could come if federal legislation authorizing the use of marijuana for medical uses is enacted into law. However, attempts to do so have not been successful.[9] The most recently proposed bill, the Medical Marijuana Patient Protection Act (H.R. 2835) introduced in 2009, would allow marijuana to be used by patients with a prescription for it in states where it is allowed under state law.[9] "The bill would move marijuana from Schedule I to Schedule II of the CSA and exempt from federal prosecution authorized patients and medical marijuana providers who are acting in accordance with state laws."[9] A Schedule II drug has a high potential for abuse, has an accepted medical use in treatment in the U.S., and abuse of the drug may lead to severe dependence.[10]

The federal Truth in Trials Act (H.R. 3939), also introduced in 2009, would allow people brought before a federal court for using or providing medical marijuana to "reveal to juries that their marijuana activity was medically related and legal under state law."[9]

Select Positions on Medical Marijuana

Several health professional organizations, many state health professional organizations, and several HIV/AIDS organizations favor the medical use of marijuana and/or further research into its effectiveness.[21]

Pro or Conditional Support

The IOM is conditionally in favor of marijuana use for certain patients until a fast-acting synthetic cannabinoid can be developed because "there is no clear alternative for people suffering from chronic conditions that might be relieved by smoking marijuana, such as pain or AIDS wasting."[5]

The American Nurses Association supports educating health care providers on medical marijuana and THC; protecting patients and health care providers from penalties associated with medical marijuana in states where it is allowed; "reclassifying marijuana from a Schedule I controlled substance to another category"; and confirming marijuana's therapeutic effect.[22]

The American Academy of Family Physicians "opposes the use of marijuana except under medical supervision and control for specific medical indications."[23] The American College of Physicians supports medical marijuana research, encour-

ages patients to use proven nonsmoked THC, "supports the current process for obtaining federal research-grade cannabis;" urges reviewing marijuana as a schedule I controlled substance; and strongly supports exempting physicians and patients from criminal, civil, and professional penalties for using marijuana as allowed under state laws.[24]

Research on cannabinoids and methods, other than smoking, to administer medical marijuana is encouraged by the American Public Health Association (APHA).[25] APHA also calls for making "cannabis available as a legal medicine where shown to be safe and effective and to immediately allow access to therapeutic cannabis through the Investigational New Drug Program."[25]

The Federation of American Scientists supports patients' cannabis use, calling for the enrollment of seriously ill patients in clinical trials if their "physicians believe that whole cannabis would be helpful to their conditions."[26]

Con

Federal agencies oppose the use of marijuana for medical purposes. In a 2006 Interagency Advisory on Smoked Marijuana as Medicine, the FDA, DEA, and ONDCP stated that a past evaluation by Department of Health and Human Services agencies found that "no sound scientific studies supported medical use of marijuana for treatment in the United States, and no animal or human data supported the safety or efficacy of marijuana for general medicinal use."[11]

Marijuana was removed from the U.S. Pharmacopoeia in 1941.[27]

The National Multiple Sclerosis Society (MS) and the Cleveland Clinic do not recommend that MS patients use medical marijuana to manage their symptoms.[28,29]

Neutral

The Veterans Health Administration (VHA) is balancing between the pro and con sides — acknowledging that some patients will choose to use marijuana, especially where its medical use is legal under state law, and the federal law that prohibits its use.

VHA issued a directive in 2010 that prohibits a Department of Veterans Affairs (VA) provider from completing forms for veterans seeking recommendations or opinions on participation in a state medical marijuana program.[30] A VA provider or pharmacist is not allowed to fill a marijuana prescription nor will the VA pay for the prescription to be filled outside of the VA system.[30] A veteran who uses medical marijuana will not be denied VHA services but may have his or her treatment plan modified.[30]

A VHA medical marijuana clinical considerations document released in 2010 suggests that providers make patients aware of marijuana's health effects, withdrawal symptoms, and use disorders and of other treatment options for patients' symptoms.[31] "Veterans may be restricted from participating in some clinical programs when smoking any substance is an exclusion criterion (for example, organ transplant programs)."[31]

Implications for Pharmacy Practice

Health-system pharmacists may find themselves asked to dispense marijuana and provide medication therapy management for patients using marijuana medicinally if states, such as New Jersey, decide that marijuana must be dispensed by hospitals rather than stand-alone dispensaries.

As marijuana becomes increasingly available to patients through state-authorized channels, pharmacists should prepare themselves to counsel patients who are considering or are already using marijuana. The **Appendix** offers tips for pharmacists concerned about how to approach this issue.[32]

Conclusion

An increasing number of states are allowing marijuana to be prescribed. Although it is used to treat symptoms like chronic pain, nausea caused by cancer treatments, and AIDS wasting, it is not considered by the federal government to have an accepted medical use. As a Schedule I controlled substance, with only one federally authorized producer, it is difficult for researchers to legally obtain marijuana for research into its effects and suitability for medical use. Several national organizations have called for additional marijuana research to learn more about its therapeutic effects.

The American Society of Health-System Pharmacists (ASHP) is considering proposed policy on medical marijuana that suggests further research into its effects when used to treat disease symptoms. Also under consideration is whether marijuana should remain a Schedule I controlled substance as the research is being done unless further research is not possible without moving it to a Schedule II controlled substance classification.

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Appendix

An *American Journal of Health-System Pharmacy* clinical review article provides the following tips for pharmacists concerned about medical marijuana. [32]

1. Keep abreast of local, state, and federal laws regarding medical marijuana.
2. When practicing in areas with medical marijuana laws, know all relevant procedures and protocols.
3. Develop a working knowledge of the risks and benefits of medical marijuana.
4. Conduct thorough medical and social histories and inquire about illicit drug use, including medical marijuana.
5. Consider patients treated for serious and chronic debilitating conditions as possible users of medical marijuana.
6. Screen patients who use medical marijuana or are inclined to use it for drug–drug and drug–disease interactions and counsel them accordingly.
7. Advise patients with psychological disease or a tendency toward addiction against marijuana use.
8. Ensure that patients using marijuana for medical purposes are under appropriate and continuous medical supervision and have met all statutory requirements.
9. Develop the necessary literature retrieval and evaluation skills to address drug information questions involving medical marijuana.
10. Never recommend a source of or provide specific instructions on how to obtain marijuana.

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