

Authorizing Dried Cannabis for Chronic Pain or Anxiety

PRELIMINARY GUIDANCE

This guidance document was prepared on behalf of the College of Family Physicians of Canada (CFPC) by members of the Addiction Medicine and Chronic Pain Program Committees, in collaboration with members of the Child and Adolescent Health, Maternity and Newborn Care, Mental Health, Palliative Care, and Respiratory Medicine Program Committees, of CFPC's Section of Family Physicians with Special Interests or Focused Practices.

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Disclaimer

This document has been prepared by the CFPC to provide preliminary, rather than comprehensive, guidance, based on what is currently known about the use of cannabis for certain medical purposes. Dried cannabis is not an approved drug or medicine in Canada, and the provision of this information should not be interpreted as an endorsement of the use of this product, or of cannabis generally, by the CFPC.

The content within this document is provided for information and education purposes about a new and largely unstudied area of clinical practice. It is not intended to substitute for the advice of a physician. Patients should always consult their doctors for specific information on personal health matters, or other relevant professionals to ensure that their own circumstances are considered.

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Contact us

The College of Family Physicians of Canada welcomes your feedback.

We are working to ensure that the recommendations in this guidance document continue to reflect the latest available evidence and to incorporate the practice expertise of CFPC members who use them.

If you have suggestions for additions or changes to this document, we would appreciate receiving them. All feedback received will be considered for inclusion in the revised guide, to be released Winter 2015.

Please forward your suggestions to healthpolicy@cfpc.ca.

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Introduction

The Health Canada Marihuana for Medical Purposes Regulations (MMPR),¹ which came into force on April 1, 2014, permit a physician to sign a medical document authorizing a patient's access to, and the dispensing of, a specified quantity of the dried cannabis plant, which patients purchase through a licensed producer. The medical document has a format and function similar to a prescription. However, dried cannabis differs from prescribed products in that Health Canada has not reviewed data on its safety or effectiveness and has not approved it for therapeutic use.

This situation puts family physicians in a difficult position: we are asked to authorize our patients' access to a product with little evidence to support its use, and in the absence of regulatory oversight and approval.

To address this predicament, this document offers family physicians preliminary guidance on the authorizing of dried cannabis for chronic pain or anxiety, pending the development of formal guidelines. Although the MMPR speak only of use for medical purposes without specifying any diagnoses, the writing group chose chronic pain and anxiety as the clinical areas to highlight because they may be the most common conditions for which a patient requests authorization for cannabis from a family physician.

Research shows that dried cannabis is a potent, psychoactive substance that can have significant acute and chronic cognitive effects. Its acute effects include perceptual distortions, cognitive impairment, euphoria, and anxiety.² Chronic use of dried cannabis may be associated with persistent neuropsychological deficits, even after a period of abstinence.^{3,4} The patient may report initial benefit from smoking cannabis and, as with many mood-altering substances such as alcohol, opioids, benzodiazepines, and cocaine, experience temporary relief from pain or anxiety. However, these products have the potential to cause harm by impairing memory and cognition, worsening performance at work and school, and by interfering with social relationships. Before authorizing cannabis, family physicians need to consider if there is sufficient evidence that the anticipated therapeutic benefits for the patient's particular health condition outweigh the potential harms. Similarly, continuation of the cannabis is warranted only if the authorizing physician is satisfied that there has been improvement in the patient's pain level, function, and/or quality of life, and that there are no signs that the patient is at risk of misuse or harm.

Methods

This document was written by members of the Addiction Medicine and Chronic Pain Program Committees of the Section of Family Physicians with Special Interests or Focused Practices (SIFP) of the College of Family Physicians of Canada (CFPC), in collaboration with other individuals and SIFP Program Committees: Child and Adolescent Health, Maternity and Newborn Care, Mental Health, Palliative Care, and Respiratory Medicine. CFPC Program Committees are made up of members with a special interest, and often enhanced expertise, in a specific clinical domain that is relevant to the practice of family medicine.

The writing team based the document on a literature search and review of evidence on specific topics related to cannabis effectiveness, safety, and adverse effects. The team acknowledges the research of Kahan and colleagues,⁵ which has been adapted in the preparation of this document. The material appears with the permission of the publisher, Canadian Family Physician.

Members of the participating program committees collaborated to prepare a succession of drafts, which then underwent review by an editorial team. A subgroup of the editorial team wrote the final document on behalf of the participants. The final document was taken to the entire group for its consensus before publication.

Recommendations were graded as Level I (based on well-conducted controlled trials or meta-analyses), Level II (well-conducted observational studies), or Level III (expert opinion; for the purposes of this document, consensus among the committee members drafting this document on behalf of the CFPC).

The context within which the participants worked to produce this document is extraordinary, as we have described above: authorization of a largely unstudied substance, particularly challenging medical practice areas (pain and addiction), intense interest from patients (often accompanied by less interest in evidence), an absence of regulation, and, above all, an urgency to provide basic parameters to guide family physicians in the safe treatment of their patients.

The individuals named in the Acknowledgements agreed to be listed as contributors on the basis that this document:

- Was urgently needed to address a knowledge gap in a controversial practice area without the usual supports and
- Provides preliminary guidance while the CFPC engages in a rigorous process to provide more formal clinical practice guidelines and continuing professional development offerings

Terminology

Medical marijuana: This term is in popular use but is imprecise, referring broadly to dried cannabis dispensed or otherwise obtained and used either for supervised medical purposes or for self-medication. In a scientific context we prefer to use the term "dried cannabis."

Dried cannabis/cannabis: We use these terms interchangeably to refer to the substance under discussion in this paper: the product that a patient may purchase through a licensed producer, under the MMPR, if he or she has a medical document authorizing its dispensing.

Pharmaceutical cannabinoids: This term refers to the prescription drugs nabilone (Cesamet) and nabiximols (Sativex). Marinol (dronabinol) was previously available but has been removed from the Canadian market by the manufacturer.

Medical document: Health Canada uses this term to denote the prescription-like form that physicians complete and sign to authorize patients' access to dried cannabis from licensed producers. Health Canada provides a sample medical document on its website.6

How to navigate this document

This document is organized into two parts. The first, "A. Summary of Recommendations," outlines the recommendations in brief, sketching in point form the new and still developing landscape within which family physicians find themselves regarding "medical marijuana":

- The federal regulations that give the physician the responsibility for granting access to this unregulated substance
- The as-yet limited evidence regarding cannabis's effects and efficacy in clinical use
- The degree to which evidence derived from studies of pharmaceutical cannabinoids can be applied to dried cannabis, and vice versa
- The provincial medical regulatory authorities' requirements of physicians regarding signing medical documents for cannabis
- The issues and questions that arise in the sometimes challenging conversations between physicians and patients surrounding cannabis

The second part, "B. Discussion and Supporting Evidence," provides a fuller discussion of these topics. It describes:

- What we know to date about the potential harms and benefits of cannabis use in various populations and for treating different conditions, with a focus on pain and anxiety
- Regulations and suggested best practices to follow before authorizing and continuing a patient's access to cannabis

It also provides practical resources to use in clinical practice, including:

- Messages for patients
- Tools to use when screening patients for misuse or addiction risk
- A sample treatment agreement
- Information about the strains available from licensed producers
- Calculations for dosing

In sections A and B, the recommendations are grouped under the headings:

- General principles (recommendations 1–6)
- Misuse prevention and intervention (recommendation 7)
- Assessment, monitoring, and discontinuation (recommendations 8 and 9)
- Strategies to prevent harm (recommendations 10 and 11)
- Communication with patients and consultants (recommendations 12 and 13)
- Dosing (recommendations 14 and 15)

A. Summary of Recommendations

To navigate to the discussion and evidence for an individual recommendation, click on the hyperlinked heading.

General principles

Recommendation 1

There is no research evidence to support the authorization of dried cannabis as a treatment for pain conditions commonly seen in primary care, such as fibromyalgia or low back pain (Level III). Authorizations for dried cannabis should only be considered for patients with neuropathic pain that has failed to respond to standard treatments (Level I).

Recommendation 2

If considering authorizing dried cannabis for treatment of neuropathic pain, the physician should first consider a) adequate trials of other pharmacologic and nonpharmacologic therapies and b) an adequate trial of pharmaceutical cannabinoids (Level I).

Recommendation 3

Dried cannabis is not an appropriate therapy for anxiety or insomnia (Level II).

Recommendation 4

Dried cannabis is not appropriate for patients who:

- a) Are under the age of 25 (Level II)
- b) Have a personal history or strong family history of psychosis (Level II)
- c) Have a current or past cannabis use disorder (Level III)
- d) Have an active substance use disorder (Level III)
- e) Have cardiovascular disease (angina, peripheral vascular disease, cerebrovascular disease, arrhythmias) (Level III)
- Have respiratory disease (Level III) or f)
- Are pregnant, planning to become pregnant, or breastfeeding (Level II)

Recommendation 5

Dried cannabis should be authorized with caution in those patients who:

- a) Have a concurrent active mood or anxiety disorder (Level II)
- b) Smoke tobacco (Level II)
- c) Have risk factors for cardiovascular disease (Level III) or
- d) Are heavy users of alcohol or taking high doses of opioids or benzodiazepines or other sedating medications prescribed or available over the counter (Level III)

Recommendation 6

Physicians should follow the regulations of their provincial medical regulators when authorizing dried cannabis (Level III).

Misuse prevention and intervention

Recommendation 7

Physicians should assess and monitor all patients on cannabis therapy for potential misuse or abuse (Level III).

Assessment, monitoring, and discontinuation

Recommendation 8

Before signing a medical document authorizing dried cannabis for pain, the physician should do all of the following:

- a) Conduct a pain assessment (Level II)
- b) Assess the patient for anxiety and mood disorders (Level II)
- c) Screen and assess the patient for substance use disorders (Level II)

Recommendation 9

The physician should regularly monitor the patient's response to treatment with dried cannabis, considering the patient's function and quality of life in addition to pain relief (Level III). The physician should discontinue authorization if the therapy is not clearly effective or is causing the patient harm (Level III).

Strategies to prevent harm

Recommendation 10

Patients taking dried cannabis should be advised not to drive for at least:

- a) Four hours after inhalation (Level II)
- b) Six hours after oral ingestion (Level II)
- c) Eight hours after inhalation or oral ingestion if the patient experiences euphoria (Level II)

Recommendation 11

When authorizing dried cannabis therapy for a patient, the physician should advise the patient of harm reduction strategies (Level III).

Communication with patients and consultants

Recommendation 12

The physician should manage disagreements with patients about decisions around authorization, dosing, or other issues with unambiguous, evidence-based statements (Level III).

Recommendation 13

The physician who is authorizing cannabis for a particular clinical indication must be primarily responsible for managing the care for that condition and following up with the patient regularly (Level III). Physicians seeking a second opinion on the potential clinical use of cannabis for their patient should only refer to facilities that meet standards for quality of care typically applied to specialized pain clinics (Level III). In both instances, it is essential that the authorizing physician, if not the patient's most responsible health care provider, communicate regularly with the family physician providing ongoing comprehensive care for the patient (Level III).

Dosing

Recommendation 14

Given the weak evidence for benefit and the known risks of using cannabis, the only sensible advice for physicians involved with authorizing dried cannabis is the maxim "Start low, and go slow" (Level III).

Recommendation 15

Although it is not required by the MMPR, physicians should specify the percentage of THC on the medical document for all authorizations for dried cannabis, just as they would specify dosing when prescribing any other analgesic (Level III).

B. Discussion and Supporting Evidence

General principles

RECOMMENDATION 1

There is no research evidence to support the authorization of dried cannabis as a treatment for pain conditions commonly seen in primary care, such as fibromyalgia or low back pain (Level III). Authorizations for dried cannabis should only be considered for patients with neuropathic pain that has failed to respond to standard treatments (Level I).

To date, five controlled trials have examined dried cannabis in the treatment of chronic neuropathic pain. 7-11 The trials were small, included patients who had previously smoked cannabis, and lasted from 1 to 15 days. Functional status, quality of life, and other important outcomes were not measured. No head-to-head comparisons of therapeutic benefits or adverse effects were made with other standard treatments for these conditions, or with pharmaceutical cannabinoid preparations.

The safety and effectiveness of dried cannabis has not been studied for pain conditions such as fibromyalgia and low back pain. No controlled studies have been conducted on dried cannabis for osteoarthritis, and the Canadian Rheumatology Association does not endorse the use of dried cannabis for either fibromyalgia or osteoarthritis.¹² The oral pharmaceutical cannabinoid nabilone has some evidence of benefit for these conditions, although the evidence is weaker than for first-line treatments. 13,14 Family physicians are advised to recommend other treatments with more evidence of safety and efficacy for these conditions.

RECOMMENDATION 2

If considering authorizing dried cannabis for treatment of neuropathic pain, the physician should first consider a) adequate trials of other pharmacologic and nonpharmacologic therapies and b) an adequate trial of pharmaceutical cannabinoids (Level I).

There are many pharmacologic and nonpharmacologic treatments documented as effective in the treatment of neuropathic pain, and these established therapies should be tried before moving on to trials of cannabinoids. Oral and buccal pharmaceutical cannabinoids have a larger body of evidence of efficacy than has dried cannabis in the treatment of neuropathic pain, 15-20 although, apart from Sativex (indicated for neuropathic pain associated with multiple sclerosis or cancer), these drugs' use for this treatment is off label. Evidence suggests that oral cannabinoids are also safer, with a lower risk of addiction and with milder cognitive effects. 19,21-27

However, until further research is conducted, the same contraindications and precautions that apply to dried cannabis apply to pharmaceutical cannabinoids. Patients who request cannabis but refuse a trial of pharmaceutical cannabinoids may be using cannabis for euphoria rather than analgesia.

RECOMMENDATION 3

Dried cannabis is not an appropriate therapy for anxiety or insomnia (Level II).

To our knowledge, there have been no controlled studies to date on the use of dried cannabis in the treatment of anxiety disorders. There is, however, a strong and consistent association between cannabis use and anxiety and mood disorders, although causality has not been established.²⁸⁻³⁸ Acute cannabis use can trigger anxiety and panic attacks,³⁹ and studies on animals and human volunteers suggest that high doses of cannabis actually worsen anxiety.⁴⁰ Cannabis use may worsen psychiatric impairment in patients with anxiety disorders.^{36,41,42}

The tetrahydrocannabinol (THC) content of cannabis is associated with anxiety,⁴¹ though this relationship appears to be bidirectional.^{43,44} Physicians should consider the THC content of available cannabis and consider authorizing, if at all, only lower-strength strains for patients with anxiety.⁴⁵ Regular users of cannabis might experience early symptoms of cannabis withdrawal, including an exacerbation of anxiety, when they abstain; withdrawal symptoms can ultimately be resolved through cannabis cessation.⁴⁶

The evidence for using pharmaceutical cannabinoids in the treatment of anxiety and insomnia is stronger than the evidence for using dried cannabis. Small trials have demonstrated that oral nabilone improves sleep in patients with fibromyalgia or post-traumatic stress disorder. An oral extract of pure cannabidiol has been shown to relieve symptoms of social anxiety.

RECOMMENDATION 4

Dried cannabis is not appropriate for patients who:

- a) Are under the age of 25 (Level II)
- b) Have a personal history or strong family history of psychosis (Level II)
- c) Have a current or past cannabis use disorder (Level III)
- d) Have an active substance use disorder (Level III)
- e) Have cardiovascular disease (angina, peripheral vascular disease, cerebrovascular disease, arrhythmias) (Level III)
- f) Have respiratory disease (Level III) or
- g) Are pregnant, planning to become pregnant, or breastfeeding (Level II)

Patients under the age of 25 (Level II)

Youth who smoke cannabis are at greater risk than older adults for cannabis-related psychosocial harms, including suicidal ideation, illicit drug use, cannabis use disorder, and long-term cognitive impairment.^{4,33,49-52}

Patients with current, past, or strong family history of psychosis (Level II)

Observational studies have demonstrated a consistent association between cannabis use in adolescence and persistent psychosis.⁵³⁻⁶⁰

Patients with current or past cannabis use disorder (Level III)

Pain patients with cannabis use disorder should be counseled to discontinue cannabis and be referred for addiction treatment.

Patients with an active substance use disorder (Level III)

Dried cannabis should not be authorized for any patient with a current problematic use of alcohol, opioids, or other drugs.

Patients with cardiovascular disease (Level III)

Cannabis use causes acute physiological effects such as hypertension, tachycardia, catecholamine release, and vascular constriction.⁶¹⁻⁶⁴ There have been reports of young people suffering cardiovascular events shortly after smoking cannabis. 65-67

Patients with respiratory disease (Level III)

Heavy cannabis smoking may be an independent risk factor for impaired respiratory function and chronic obstructive pulmonary disease. 68,69

Use of smoked cannabinoids has been found to increase the risk of airflow obstruction and hyperinflation but has been less associated with macroscopic emphysema. 70 The cannabis use was associated with increased risk of lung cancer⁷¹ and head and neck cancer.⁷² The respiratory symptoms associated with dried cannabis use include wheezing apart from colds, exercise-induced shortness of breath, nocturnal wakening with chest tightness, and early morning sputum production.⁷³

The depth of inhalation and the length of time the breath is held are usually greater when smoking marijuana than when smoking cigarettes. This means exposure to the chemicals in the smoke is greater for cannabis than for tobacco cigarettes, even though the frequency of smoking may be less. Cannabis smokers, for example, end up with five times more carbon monoxide in their bloodstream than do tobacco smokers.⁷¹

Patients who are pregnant, planning to become pregnant, or breastfeeding (Level II) Preliminary evidence links cannabis use during pregnancy to neurodevelopmental abnormalities in infants.⁷⁴ Cannabis enters the breast milk and is contraindicated in women who are breastfeeding.

RECOMMENDATION 5

Dried cannabis should be authorized with caution in those patients who:

- a) Have a concurrent active mood or anxiety disorder (Level II)
- b) Smoke tobacco (Level II)
- c) Have risk factors for cardiovascular disease (Level III) or
- d) Are heavy users of alcohol or taking high doses of opioids or benzodiazepines or other sedating medications prescribed or available over the counter (Level III)

Patients with current mood and anxiety disorders (Level II)

Caution should be used when authorizing cannabis for patients with current mood or anxiety disorders, for the reasons outlined in **Recommendation 3**. If patients with co-existing anxiety and neuropathic pain are authorized for cannabis treatment, i) the dose should be kept low to avoid triggering anxiety, ii) the provider should consider indicating low THC-content or cannabidiol-only (CBD-only) strains on the medical document, and iii) cannabis should be discontinued if the patient's anxiety or mood worsens.

Tobacco smokers (Level II)

Even after controlling for tobacco smoking, cannabis smoking has been associated with lung cancer⁷⁵ and chronic bronchitis. Patients who smoke tobacco should be strongly advised to use cannabis via vaporization rather than by smoking it.

Patients with risk factors for cardiovascular disease (Level II)

Physicians are advised to use considerable caution when authorizing dried cannabis for use by patients with risk factors for cardiovascular disease (see Recommendation 4e). The dose should be kept low, and the patient should be encouraged to take it through vaporization or the oral route rather than by smoking it.

Patients who are heavy users of alcohol, or taking high doses of opioids or benzodiazepines (Level III)

Cannabis use can worsen the cognitive impairment caused by opioids, benzodiazepines, other sedatives, and alcohol.⁷⁶ Patients taking dried cannabis should be advised to use alcohol in moderation, and physicians should consider tapering patients on high doses of opioids or benzodiazepines.^{77,78}

RECOMMENDATION 6

Physicians should follow the regulations of their provincial medical regulators when authorizing dried cannabis (Level III).

Many of the provincial/territorial regulatory bodies have released policies on the authorization of cannabis.⁷⁹ These regulators advise physicians to conduct a thorough assessment and to try conventional alternatives before providing a medical document for cannabis. Additional requirements, which vary considerably from province to province, are summarized below and in **Table 1**. Physicians should review the complete policy of their provincial regulator before signing a medical document for cannabis.

Conflict of interest

Physicians must not have a financial interest in a company that produces medical marijuana, and they should follow their provincial regulatory authority's Code of Ethics regarding potential conflicts of interest. Under the usual circumstances described in the MMPR, the licensed producer couriers the dried cannabis to the patient. Under extraordinary circumstances (if, for example, the patient does not have a postal address) the physician may receive and store dried cannabis. Consultation with provincial regulatory authorities about all such arrangements is advised.

Authorizations

Several provinces require physicians to:

- State the patient's medical condition on the medical document
- Register with the regulator as a cannabis authorizer
- Send the regulator a copy of the medical document, and/or keep the medical documents on a separate record for possible inspection

Some provinces specify that only the physician who manages the patient's condition may write a medical document authorizing cannabis, so that the therapy occurs in the most potentially beneficial context of continuing and comprehensive care. An ongoing doctor-patient relationship is similarly important when visits are conducted using telemedicine—where patient and physician must communicate via an interface rather than face to face. For this reason, authorization of dried cannabis by physicians not usually involved in the patient's care and using telemedicine is problematic; the authorizing physician is compelled to monitor response to treatment, emergence of adverse effects, and signs and symptoms of addiction without being physically present with the patient. This raises clear questions about whether care quality to these standards is possible in the context of a relationship that is carried out via telemedicine.

Documentation and consent

Several regulators recommend that the patient sign a written treatment agreement (see **Table 2**), that the physician document that other treatments have been tried, and that the patient is aware of the risks of dried cannabis. They also recommend that the patient be reassessed at least every three months.

Assessment and monitoring for cannabis misuse

Several provincial regulators advise physicians to use a standardized tool to assess the patient's risk of addiction, and to have a procedure or protocol for identifying cannabis misuse.

Table 1. Provincial regulatory authorities' policies on authorizing dried cannabis							
Medical Regulatory Authorities Requirements Applying to Physicians (Provincial Colleges or Councils)							
Conflict of interest	ВС	AB	SK	MB	QC	NB	NL
Must not apply to become a licensed producer		•			•		
Must not store, provide, or dispense marijuana		•	•	•	•		
Must not have any financial or management interest in a licensed distributer or producer			•				•
Must not have any personal gain from providing a non-medical service						•	
Authorizations	ВС	AB	SK	MB	QC	NB	NL
State patient's medical condition on medical document		•	•	•			
Register with regulator as a dried cannabis authorizer		•					
Provide a copy of the medical document to the regulator		•	•				
Send original medical document to licensed producer, give copy to patient, and enter another copy in chart					•		
Review available prescription databases to determine patient's medication usage	•	•					
Keep all medical documents on a separate record for inspection by the College			•	•	•		
May only sign a medical document authorizing cannabis for a patient if he or she is the primary manager of the patient's medical condition			•	•			•
May not authorize cannabis through telemedicine	•						
Keep a register of cannabis patients so they can be invited to participate in the research database projects					•		
Consent and documentation	BC	AB	SK	MB	QC	NB	NL
Inform the patient that cannabis can only be authorized as part of the research database project					•		
Ask the patient to read the patient information document					•		
Have patient sign a written treatment agreement			•		•		
Have the patient sign a written consent form	•				•		
Document that the patient was informed of the risks and benefits, and that other treatments were tried	•	•	•	•			•
Assess the patient at least every three months		•			•		
Assessment and monitoring	BC	AB	SK	MB	QC	NB	NL
Complete the assessment and follow-up form available on the regulator's website					•		
Cannabis misuse	ВС	AB	SK	MB	QC	NB	NL
Assess the patient's risk of addiction using standardized tool	•	•					•
Have a process or protocol for identifying misuse		•		•			•

Source: Canadian Consortium for the Investigation of Cannabinoids, www.ccic.net/index.php?id=248,703,0,0,1,0. Accessed 2014 Jun 17.

Please visit CFPC's website for information on the latest statements and requirements from the provincial regulatory authorities: http://www.cfpc.ca/medical_marijuana/

_	e 2. Sample treatment agreement		
	use we take our responsibilities to authorize seriously, we ask you to read, understand, a		marijuana (dried cannabis)
1.	I request Dr, MD, to sign a medical d legally use marijuana to treat my medical condition.		a MMPR legislation, so that I may
2.	I agree to receive a medical document for marijuana	a only from one physician, Dr	, MD.
3.	I agree to consume no more marijuana than the dos before the agreed-upon refill date.	es authorized for me by Dr	, MD. I will not request a refill
4.	I agree to not distribute my marijuana to any other μ marijuana for sale is an illegal activity.	person, for personal use or for sale. I am a	aware that redistribution of any
5.	I am aware that using marijuana is associated with ρ growth). Therefore, I will ensure that no person under the contract of		
6.	I agree to the safe storage of my marijuana.		
7.	I am aware that taking marijuana with other substandeath. I will not use illegal drugs (eg, cocaine, heroi not prescribed for me.		
8.	I will not use controlled substances that were prescr	ribed by another doctor unless Dr	, MD, is aware of this.
9.	I agree to testing (eg, urine drug screening) when an	d as requested by my physician.	
10.	I agree to have an office visit and medical assessmen	nt at least every (months or weeks).	
11.	I understand that Health Canada has provided access treatment of certain medical conditions, but despite in Canada.	, , ,	. ,
12.	I understand that my physician may not be knowled approved substance like marijuana.	geable about all of the risks associated w	ith the use of a non-Health Canada-
13.	I agree to communicate to my physician, Drside effects of the use of marijuana.	, MD, any experiences of altered n	nental status or possible medical
14.	I accept full responsibility for any and all risks associate effects of the product.	ciated with the use of marijuana, including	g theft, altered mental status, and
15.	I am aware that marijuana use is not advisable durin Dr, MD, if I am pregnant.	ng pregnancy and breastfeeding. I agree to	o inform my physician,
16.	I am aware that smoking any substance can cause h avoid smoking marijuana. I will avoid mixing mariju edible product.		
17.	I am aware that my physician may discontinue authomental health risk or side effects are too high.	orizing marijuana for my condition if he o	or she assesses that the medical or
18.	I agree to see specialists or therapists about my cond	dition at my physician's request.	
19.	I agree to avoid driving a vehicle or operating heavy feel any persistent negative effects on my ability to compare the second of the second o		use of marijuana, and for longer if I
20.	As per the Health Canada MMPR legislation, I agree possession of marijuana from other sources is illegal		censed producer. I am aware that
21.	I am aware that any possible criminal activity related charges may be laid. During the course of an investi a warrant.		
22.	Following the terms of this contract is one of the conviolate any of this agreement's terms, my physician is		
23.	Dr, MD, has the right to discuss members if it is felt, on balance, that my safety outw		care professionals or family
	Patient's printed name	Patient's signature	
	Date	Practitioner's signature	

Misuse prevention and intervention

RECOMMENDATION 7

Physicians should assess and monitor all patients on cannabis therapy for potential misuse or abuse (Level III).

All patients using dried cannabis regularly should be monitored carefully and assessed routinely for cannabis use disorder. Clinical features of cannabis use disorder are listed in Table 3. Patients with suspected cannabis use disorder should be advised that they will likely experience improved mood and better function if they stop or reduce their use. Patients who are unable to stop or reduce should be referred for formal addiction treatment. Cannabis should not be authorized for patients with current problematic use of cannabis, alcohol, or other drugs (see Recommendation 5d).

Before authorizing cannabis use for the patient, the physician should take a careful history of current and past substance use, including cannabis, alcohol, tobacco, prescription opioids, and benzodiazepines, and illicit drugs such as heroin and cocaine. Several medical regulatory authorities recommend using a standardized tool to assess the risk of addiction. The CAGE-AID instrument⁸⁰ is one such simple tool (Table 4). A urine drug screen may also be included in the initial assessment.

If the patient does not use substances problematically and begins cannabis treatment, the physician should ask the patient at each office visit about cognitive and mood-altering effects, as well as compliance with the dosing recommendations and use of any other substances. Periodic urine drug screens are advised.

The authorization for cannabis should be discontinued if the patient:

- Runs out early or uses cannabis from other sources
- Begins to use alcohol, opioids, or other drugs problematically
- Begins to show signs of a cannabis use disorder

Table 3. Clinical features of cannabis use disorder in patients with chronic pain

- Insists on a medical document for dried cannabis rather than trying other treatments known to be effective for his or her condition
- Uses cannabis daily or almost daily, spending considerable non-productive time on this activity
- Has poor school, work, and social functioning
- Is currently addicted to or misusing other substances (other than tobacco)
- Has risk factors for cannabis use disorder: is young, has current mood or anxiety disorder or a history of addiction or misuse
- Reports having difficulty stopping or reducing use
- · Reports cannabis withdrawal symptoms after a day or more of abstinence: intense anxiety, fatigue
- Has friends or family members concerned about his or her cannabis use

Assessment, monitoring, and discontinuation

RECOMMENDATION 8

Before signing a medical document authorizing dried cannabis for pain, the physician should do all of the following:

- a) Conduct a pain assessment (Level II)
- b) Assess the patient for anxiety and mood disorders (Level II)
- c) Screen and assess the patient for substance use disorders (Level II)

The physician should ask the patient to rate the pain on a 10-point scale, and to describe the effect of the pain on daily activities, including sleep. The physician should also assess the patient's mood. The physician should take a careful history of current and past substance use, including cannabis, alcohol, tobacco, prescription opioids and benzodiazepines, and illicit drugs such as heroin and cocaine. Several of the provincial medical regulators (the provincial licensing colleges) recommend a standardized tool to assess the risk of addiction; the CAGE-AID is one simple, validated tool⁸¹ available to physicians (**Table 4**). A urine drug screen is also advised, and the patient should be asked to read and sign a treatment agreement (**Table 2**).

RECOMMENDATION 9

The physician should regularly monitor the patient's response to treatment with dried cannabis, considering the patient's function and quality of life in addition to pain relief (Level III). The physician should discontinue authorization if the therapy is not clearly effective or is causing the patient harm (Level III).

At follow-up office visits, the physician should reassess the effects of cannabis on the patient's pain ratings and function.

Many psychoactive drugs with abuse liability will temporarily blunt the patient's perception of pain without improving function. All centrally acting analgesics can also cause sedation, euphoria, or cognitive impairment. To authorize or continue to authorize dried cannabis for the purpose of analgesia, physicians should be as certain as they would need to be in prescribing any other analgesic that its potential benefits are greater than its potential risks.

Dried cannabis therapy should be reassessed and possibly stopped in the following circumstances:

- The patient experiences insufficient analgesia and/or no improvement in function (note that some pain patients continue to complain of severe pain even as their function improves)
- The treatment is not improving sleep, mood, function, and/or quality of life
- The patient experiences side effects such as memory impairment, sedation, fatigue, and worsening functioning
- The patient shows clinical features of cannabis use disorder (Table 3), such as running out early or using cannabis from other sources

Strategies to prevent harm

RECOMMENDATION 10

Patients taking dried cannabis should be advised not to drive for at least:

- a) Four hours after inhalation (Level II)
- b) Six hours after oral ingestion (Level II)
- c) Eight hours after inhalation or oral ingestion if the patient experiences euphoria (Level II)

Cannabis use prior to driving is an independent risk factor for motor vehicle accidents. 82-86 Patients should be advised not to drive for a minimum of four hours after inhalation or a minimum of six hours after oral ingestion⁸⁷; they should abstain from driving for a full eight hours if they experience euphoria.⁸⁸

However, note that "Health Canada states that the ability to drive or perform activities requiring alertness may be impaired for up to 24 hours following a single consumption."12

RECOMMENDATION 11

When authorizing dried cannabis therapy for a patient, the physician should advise the patient of harm reduction strategies (Level III).

Some patients may consider dried cannabis to be "natural" and therefore safer than pharmaceutical products. They may be unaware that it is as important to follow dosing recommendations with dried cannabis as with any other course of treatment, and that different modes of delivery are safer or more precise than others.

For example, vaporization appears to be safer than smoking (combustion) as the vapour contains fewer toxic elements.⁸⁹ Vaporization of herbal cannabis has also been evaluated in clinical trials.⁹⁰ One such vaporizer is approved as a medical device in Canada (the Volcano Medic). 91 However, long-term safety effects of unregulated cannabis vaporization techniques (such as e-cigarettes) are unknown at this time.

It is important to ensure that patients understand that potential side effects of cannabis, such as sedation or cognitive impairment, can impact their safety. As noted in Recommendation 10, Health Canada has stated that driving, operating heavy equipment, or other activities involving alertness and coordination may be unsafe for up to 24 hours following a single consumption, depending on the dosage, delivery route, and patient's age and other health factors. It is important to discuss with patients that their reactions to the substance and to different formulations are individual, and that it is important to go slowly with the treatment until a stable, effective dose is reached.

We advise physicians to share patient education materials, such as the strategies in **Table 5**, with the patients they authorize for dried cannabis treatment.

Communication with patients and consultants

RECOMMENDATION 12

The physician should manage disagreements with patients about decisions around authorization, dosing, or other issues with unambiguous, evidence-based statements (Level III).

The main messages for the patient who requests cannabis are that a) cannabis is not an approved medicine and b) the medical literature to date reports little evidence of benefit and considerable risk of harm with its use (see **Table 6**).

Have you ever felt you ought to Cut down on your drinking or drug use? Have people Annoyed you by criticizing your drinking or drug use?
Have people Annoyed you by criticizing your drinking or drug use?
Have you ever felt bad or G uilty about your drinking or drug use?
Have you ever had a drink or used drugs first thing in the morning (Eye-opener) to steady your nerves, get rid of a hangover, or get the day started?
•

Table 5. Advice for patients about safety and harm reduction

- Use the lowest dose necessary.
- Do not "breath hold" or take more cannabis than the dose your doctor has specified.
- We recommend you ingest (that is, eat) your cannabis or take it using a vaporizer instead of smoking it, to reduce your risk of exposure to toxins that result from burning the cannabis in a cigarette. This is important to help protect you from heart or lung disease.
- Do not use dried cannabis with alcohol or other sedating drugs.
- If you are smoking cannabis, do not mix tobacco into the cigarette.
- Do not give or sell your cannabis to others—it is both dangerous and illegal.
- Store your dried cannabis in a locked container, out of reach of children and hidden from visitors and from adolescents at home.
- Avoid smoking cannabis in your house, to limit exposure of family members to second-hand smoke.
- Do not drive for at least four hours after any use by any route, and for at least six hours after oral ingestion. Do not drive for at least eight hours after using cannabis if you experience euphoria when you use it.
- · Do not use cannabis of any kind if you are pregnant or plan to become pregnant, or if you are breastfeeding.

Table 6. Messages to patients who disagree with your decision to not authorize cannabis treatment

- Dried cannabis is not a good treatment for you, even if you experience less anxiety or pain right after use. Overall, it may be harming you. It can cause sedation and fatigue, depression, anxiety, or memory impairment. It can also interfere with your work, school, or social relationships.
- Dried cannabis has some serious risks and there is little evidence of benefit.
- Neither Health Canada nor any national medical organization has endorsed dried cannabis as a medicine. As a doctor I am bound to comply with the standards of my profession.
- We will work together to come up with an individualized treatment plan for you. Safe and effective treatments are available for your condition.
- If the patient is at high risk for cannabis-related harms, eg, is young or has a concurrent anxiety or substance use disorder: As your doctor I cannot prescribe any treatment that may harm you.
- If the patient refuses a trial of oral cannabinoids prior to any consideration of dried cannabis, explore the possibility that the patient is using dried cannabis for its effects on mood: If these drugs are not helping with pain relief or function, is it possible that you are getting a high from cannabis that makes it seem like it is helping pain for a while? If that's so, the trouble is that the high can also impair your thinking and perception, which can create bigger problems for you.
- If the patient remains dissatisfied: I can't authorize the use of an untested therapy when we have other, carefully studied and effective treatments that are safer and subject to strict quality control. I won't authorize dried cannabis for you. I can refer you to a doctor who is a pain specialist, who can advise you on the risks and benefits of dried cannabis for your condition.
- If you suspect a cannabis use disorder: In my opinion, your use of cannabis could be causing you harm. We need to talk about ways to reduce or stop your cannabis use.
- If the patient says that your refusal forces him or her to purchase cannabis illegally: I advise you not to buy cannabis or any other drug from the street. In my opinion, using street cannabis is not benefiting your health, and it could be causing you harm.

RECOMMENDATION 13

The physician who is authorizing cannabis for a particular clinical indication must be primarily responsible for managing the care for that condition and following up with the patient regularly (Level III). Physicians seeking a second opinion on the potential clinical use of cannabis for their patient should only refer to facilities that meet standards for quality of care typically applied to specialized pain clinics (Level III). In both instances, it is essential that the authorizing physician, if not the patient's most responsible health care provider, communicate regularly with the family physician providing ongoing comprehensive care for the patient (Level III).

Fragmentation of patient care is never advisable. Several regulatory authorities (see Recommendation 6) have advised that authorization of cannabis and care for a clinical condition that includes cannabis therapy should be managed by the most responsible health care provider for that patient.

Before referring a patient, the physician should first ensure that the clinic:

- a) Has expertise in the patient's medical or psychiatric condition
- b) Routinely conducts a careful patient assessment prior to recommending any therapeutic intervention

- c) Provides an explicit statement on the clinic's policies on the indications, contraindications, and dosing for dried cannabis
- d) Does not have any financial conflicts of interest, such as charging patients fees, or financial involvement with licensed cannabis producers

The referring physician should send the consultant all clinically relevant information on the patient's substance use, mental health, and pain history.

Dosing

RECOMMENDATION 14

Given the weak evidence for benefit and the known risks of using cannabis, the only sensible advice for physicians involved with authorizing dried cannabis is the maxim "Start low, and go slow" (Level III).

The optimal dose should improve pain relief and function, while causing minimal euphoria or cognitive impairment. Gradual dose titration is needed to establish the dose's effectiveness and safety. This is of critical importance because, as Health Canada has stated, even low doses of low-THC cannabis can cause cognitive impairment lasting as long as 24 hours in some individuals.^{2,12}

What follows is a synthesis of what we know from the few controlled trials on dried cannabis available, and the medical literature on pharmaceutical cannabinoids. In the absence of rigorous evidence, we cannot overstress the importance of exhausting other possible therapies before embarking on a trial of cannabis therapy, as well as the necessity to "start low and go slow," while continually monitoring the patient's response to the treatment.

Suggested dosing: start low

Determining a safe and effective dose for herbal cannabis is much more difficult than for pharmaceutical products, because individuals vary in their mode of administration (eg, inhaled versus oral), so that there can be a wide variation in the dose delivered. Wide interpatient dose variability is also noted for pharmaceutical cannabinoids.⁹²

Subjects in one trial experienced relief of pain with one inhalation of 9.4% THC cannabis smoked three times per day. The single inhalation produced a serum level of 45 μ g/L,¹¹ a level slightly lower than the level associated with euphoria (50–100 μ g/L).

Patients initiating cannabis therapy in inhaled form (smoked or vaporized) should start with very small amounts of herbal cannabis. Patients often measure their "dose" in terms of puffs; a single inhalation therefore represents a meaningful and intuitive "dose" form. Since the products available to the patient vary in the amount of cannabinoid they contain (cannabis strains have different cannabinoid profiles), by starting with a single inhalation of a new strain, the patient may slowly explore his or her response to the product. Starting with strains with lower THC levels is wise, because the lower percentage minimizes potential unwanted cognitive effects; higher doses of THC do not necessarily lead to better pain control.

Since medical documents need to specify 30-day quantities, and authorization takes effect on the date of signing, patients may order several grams over a one-month period; they may choose to purchase only a few grams of a given strain for two weeks, then to ask for a different strain. As long as they do not exceed the allowable 30-day limit, and are able to work with the licensed producer, patients may explore different THC and CBD profiles. The licensed producer may call the authorizing physician to confirm details of the authorization. We suggest requesting notification from the licensed producer whenever changes are made to what the physician has authorized (see **Recommendation 15**).

There are many reports of patients having to use larger quantities of herbal cannabis in the form of juicing (ie, maceration in a blender with liquids) or to prepare oral products; we simply do not have enough information to support these claims.

The following calculations are offered as preliminary pharmacokinetic considerations, based on several assumptions as outlined.

The amount of active cannabinoids delivered to the patient using herbal cannabis will depend on several factors, including the cannabinoid content of the source material and the mode of administration, as well as genetic and metabolic patient factors. Clearly the first two factors may be amenable to adjustment; the THC and CBD level of the herbal material is standardized by the licensed producers under the MMPR and physicians should suggest that patients begin with lower THC levels. The MMPR currently only allow for patients to receive dried herbal cannabis, and not any form of extract or oral edible product, so patients must also choose the mode of administration. Here the physician faces difficult choices; the inhaled route may be by vaporization, about which we have limited information, or by smoking, which is clearly not ideal but remains the most common means of cannabis self-administration.

It is useful to consider some broad considerations of these cannabis inhalation techniques to guide these discussions and decisions:

- Based on WHO estimates, an average "joint" contains 500 mg (0.5 g) of herbal cannabis. A typical tobacco cigarette, by comparison, weighs 1.0 g.
- Studies of smoked cannabis for neuropathic pain conditions suggest effective doses ranging from one single inhalation from 25 mg of herbal cannabis containing 9.4% THC three times daily using a pipe,11 to 9 inhalations from a 900 mg "joint" of herbal cannabis containing 7% THC.7,8 This translates into current evidence for a daily inhaled dose of 100-700 mg of up to 9% THC content dried cannabis.
- It is worth noting that in all studies the incidence of adverse events increases with increasing THC levels.

In the only study to date of vaporized cannabis for neuropathic pain, the amount of herbal material placed in the vaporizer was 800 mg and subjects took between 8 and 12 inhalations from the vaporizer balloon over a twohour period. Once again, analgesic effects were noted at low THC levels and side effects increased with the THC level of administered cannabis.

Most studies of smoked or vaporized cannabis use a standardized inhalation procedure: inhale slowly over 5 seconds, hold breath for 10 seconds, then gently exhale.

Until further dose and delivery system information becomes available, these data may be crudely fashioned to provide patients with the following guidance and information:

- 1. They are advised to consider using vaporized cannabis over smoked cannabis.
- They should use inhaled cannabis in a well-ventilated, private, and calm environment.
- The authorization for dried cannabis will be for the lowest effective level of THC available.
- They should start any new cannabis product with a slow single inhalation, and then wait four hours so that they can fully appreciate the effects.
- They should allow for several single inhalation trials of a product to observe and then discuss their responses with their physicians, before either increasing the number of inhalations or changing their order with the producer.
- 6. As with all psychoactive drugs, they must be informed of and alert to cannabis's potential mood-altering, euphoric, or sedative effects, which can occur and present risk even at very low doses.
- They should keep notes on effects and experiences throughout the therapy to facilitate discussion with their authorizing physician and other health professionals.

Increasing dosage: go slow

Although the MMPR allows physicians to authorize as much as 5.0 g of dried cannabis per patient per day, we expect that analgesic benefit will occur for most patients at considerably lower doses. We expect that the upper level to the safe use of dried cannabis will be on the order of 3.0 g per day, and that even this level of use should be considered only in *very circumscribed conditions*:

- This dosing level would apply to experienced users of dried cannabis only, never to cannabis-naïve patients
- It must only be arrived at through a careful process of assessing the patient's response as dosage is slowly increased, weighing analgesic benefit, improvement in function, and presence or absence of adverse effects

Furthermore, physicians considering authorizing dried cannabis at doses higher than the current evidence supports (an inhaled dose of 100–700 mg of no more than 9% THC cannabis daily) are strongly advised to:

- Discuss the decision to increase the dosage, either approaching or exceeding a 3.0 g/day level, with a trusted and experienced colleague
- Document in the patient's record the reasons that support the increased dosage

Table 7 lists the licensed producers in Canada, and the names of the strains they sell that contain 9% THC or less.⁹³

Company	Variety and Percentage THC
Bedrocan	Bediol: 6.5%
	Bedrolite: 0.5%
Canna Farms	No strains 9% or less
Cannimed	Cannimed 9.9: 9% Cannimed 1.13: 0.7%
Delta 9 biotech	Does not list % THC on website
In the Zone	Does not list % THC on website
Mettrum	Purple #2: 7.9%
	Green #1, 5: 5.5%
	Green #2: 5.5%
MedReleaf Corp	Avidekel: 1.1%
Organigram	Not listed
Peace Naturals	Harvest Moon: 9%
	Nina: 8%
Thunderbird	Not listed
Tilray	No strains 9% or less
Tweed	Argyle: 5%
Whistler	No strains 9% or less

RECOMMENDATION 15

Although it is not required by the MMPR, physicians should specify the percentage of THC on all medical documents authorizing dried cannabis, just as they would specify dosing when prescribing any other analgesic (Level III).

The THC concentrations used in the five controlled trials on neuropathic pain (see Recommendation 1) ranged from 1% to 9%. Physicians should be aware that some commercial strains have THC concentrations as high as 15%–30%; these concentrations may increase the risk of cognitive impairment.

Therefore, the physician should note on the medical document to "Supply dried cannabis containing 9% THC or less. Send information on % THC composition directly to physician's office. Notify physician of any change in THC concentration of product given to patient."

The MMPR authorization document also requires indication of a daily quantity of cannabis. As indicated above (Recommendation 14), at present, the medical literature supports a daily dose of 100-700 mg.

Conclusions

As stated earlier, the CFPC developed this guidance document in response to a clearly expressed need from members for assistance in navigating an extraordinary practice situation. They have been caught between their desire and obligation to provide evidence-informed care for their patients and a law that appears, to patients at least, to compel them to deal with dried cannabis as if it were a medicine.

For that reason, this document has been prepared with a sense of urgency. We are confident in the practice expertise and judgment of those members who participated in its creation, but recognize that the clinical conditions it deals with and the lack of solid evidence for almost any assertion in this area make giving clearcut advice difficult. We have tried, nonetheless, to provide guidance that is as definitive as possible because we recognize that family physicians will not be able to avoid making decisions when their patients approach them about this topic.

We will, as an organization, continue to support efforts by Health Canada and other bodies to generate additional research evidence on the place of dried cannabis in the treatment of chronic pain, anxiety, and the variety of other conditions for which its use has been suggested. We encourage CFPC members to contact us, to add their input and share their experiences as we move forward safely and compassionately in this new and challenging area of therapeutics.

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The following program committees of the Section of Family Physicians with Special Interests or Focused Practices endorse the final manuscript.

Addiction Medicine Child and Adolescent Health Chronic Pain

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