RHO™ PHYTO

by AVICANNA

RHO PHYTO CANADA BY AVICANNA
HEALTHCARE PRACTITIONERS GUIDE

medical cannabis by SHOPPERS™

Edition 3
March 2021

This guide provides you with information to make informed decisions about how to incorporate medical cannabis into your practice. It covers administration, dosing and titration guidance, potential side effects, warnings and precautions, and how to recommend RHO Phyto products. The purpose of this document is to provide medical information and not to serve as providing medical advice. Healthcare practitioners are responsible to exercise professional judgment when recommending the use of medical cannabis to their patients based on individual needs and circumstances. Any recommendations contained within this guide do not replace the clinical judgement of healthcare practitioners.

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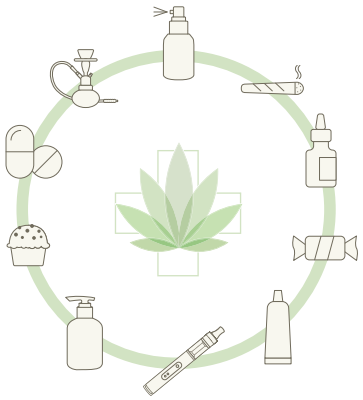
BRIEF HISTORY OF CANNABIS AS A MEDICINE

Cannabis has been used as medical treatment for millennia by many cultures with innumerable historical anecdotes of success for a wide variety of conditions, but most commonly in pain and epilepsy management. About 80 years ago, cannabis as a treatment suffered a major setback when it was deemed of no medicinal value by the World Health Organization (WHO).[1] Additionally, in 1971 the United States declared a war on drugs, ostensibly in an attempt to eradicate the drug trade and drug use. As part of this campaign, cannabis was grouped with cocaine and other more addictive substances as a Schedule 1 drug in the Controlled Substances Act.[1] As a consequence, it became difficult to conduct research on the potential of cannabis or its derivatives as medical treatments.

Figure 1. Example of various cannabis delivery forms including inhalables, orals and topicals.



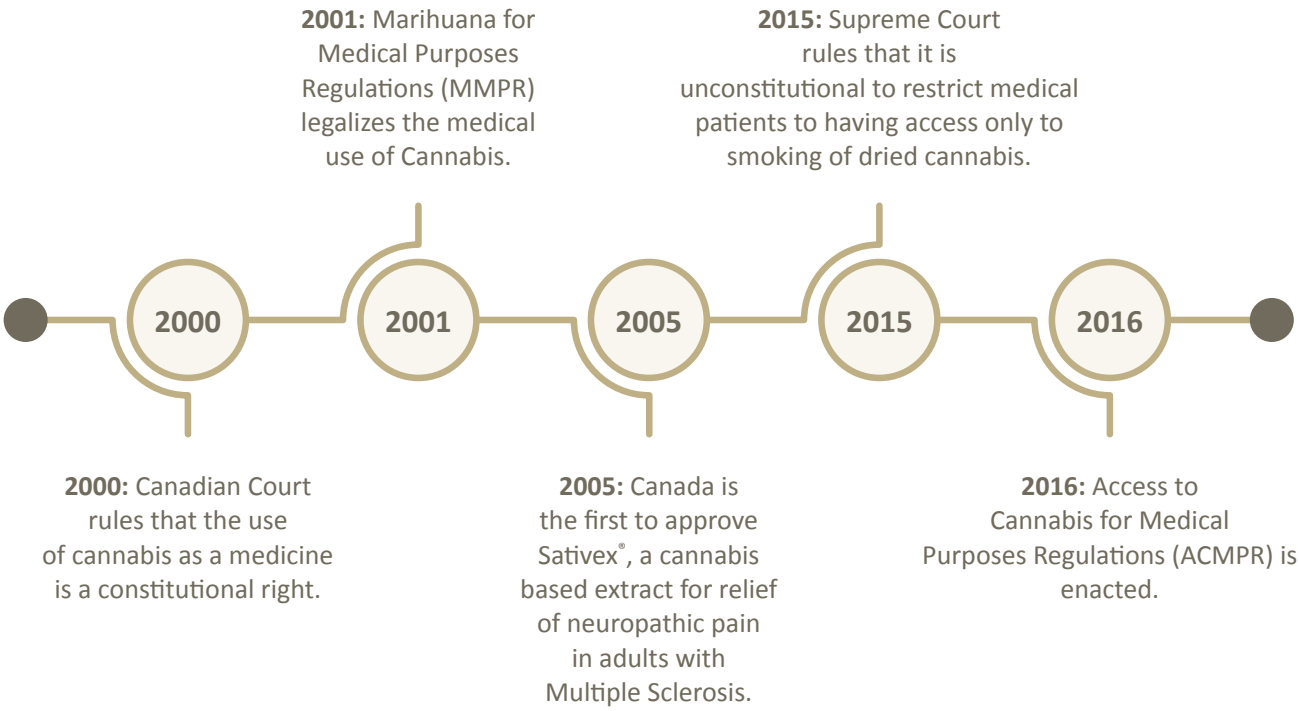
Despite this, in the ensuing years, studies were performed using whole plant extracts, cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC) isolates as treatments.[2,3] Unfortunately, most of these studies were limited by a number of methodological problems including being underpowered, poorly designed, and inadequately blinded. However, since those early studies, clinical trials have demonstrated efficacy in treating pain, spasticity, and nausea among other conditions.[4] Moreover, clinical trials have demonstrated efficacy in the context of pediatric epilepsies and with the evolving regulatory landscape it is now possible to conduct methodologically sound trials.[5]

REGULATORY FRAMEWORK FOR MEDICAL CANNABIS IN CANADA

In 1923, cannabis was added to the list of restricted drugs under the Narcotics Drug Act Amendment Bill, which prohibited Canadians from using cannabis for any purpose. However, the Canadian regulations have evolved over the past century, in part due to changing attitudes, successive court decisions, and the growing appreciation of the medical benefits of cannabis.[6] Patients demanded access to legal medical cannabis and on July 30 of 2001 the Marihuana Medical Access Regulations (MMAR) was enacted.

Finally, on October 17, 2018, the federal government passed the Cannabis Act (also known as Bill C-45), which legalized the adult-use of cannabis. An amendment to the Cannabis Act on October 17th of 2019 allowed for new classes of cannabis including cannabis extracts and topicals.

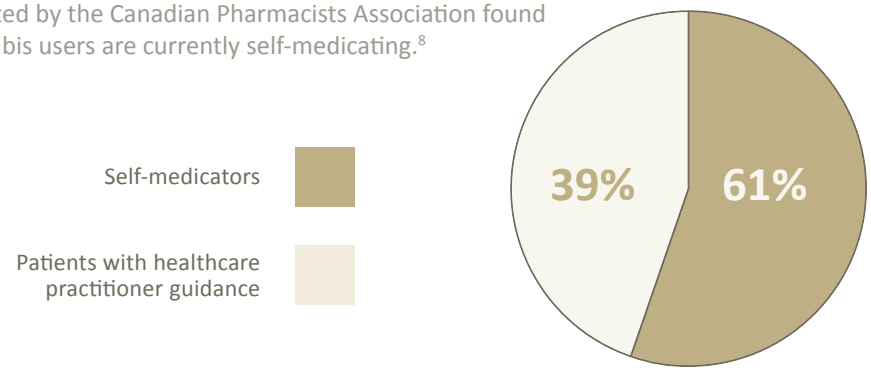
Figure 2. Brief overview of recent major milestones related to Canadian medical cannabis regulations.



MEDICAL CANNABIS USE IN CANADA

Currently, there are over 350,000 patients registered to use cannabis for medical purposes.[7] Yet, the Canadian Pharmacists Association reported that 61% of medical cannabis users are self-medicating without the guidance of healthcare practitioners (HCP).[8] Prior to January 2020, the medical products available for patients were extremely limited, with product offerings consisting mainly of dried flower and basic oil drops. However, novel delivery forms and more advanced formulations can provide patients with other options. Indeed, over 75% of patients prefer smokeless and non-inhalation product alternatives for medical use.[8]

Figure 3. A survey completed by the Canadian Pharmacists Association found that 61% of medical cannabis users are currently self-medicating.[8]



AN INTRODUCTION TO CANNABINOIDS

Endocannabinoids are natural chemical messengers that are produced by the body and interact with cannabinoid receptors and proteins within our endocannabinoid system (ECS).[9] Cannabinoid receptors are found throughout the body including the central and peripheral nervous system, cardiovascular system, liver, kidney, gastrointestinal tract, reproductive system and in the skin.[9] The balance, or homeostasis, of our ECS is maintained through interactions between the cannabinoid receptors and endocannabinoids.[10] In particular, the ECS helps regulate multiple processes including pain, appetite, digestion, sleep, mood, inflammation, and memory.[9,10]

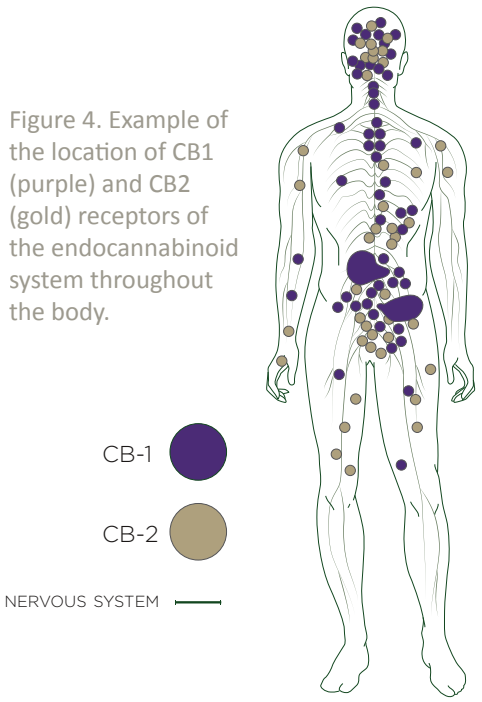


Figure 4. Example of the location of CB1 (purple) and CB2 (gold) receptors of the endocannabinoid system throughout the body.

Phytocannabinoids are found in many plants, but the highest concentrations are found in cannabis. There are over 100 known phytocannabinoids produced in the cannabis plant that have been shown to interact with the ECS.[11] The most well-known phytocannabinoids are Tetrahydrocannabinol (THC) and Cannabidiol (CBD).[12] THC, is known for its psychoactive effect or "high" sensation that alters mood or mental state. In contrast, CBD is non-psychoactive, meaning it does not produce a "high" feeling.

Table 1. Overview of the benefits of THC and CBD.[13,14]

	THC	CBD
Have been shown to help with:[5]	• Pain • Nausea and vomiting • Appetite	• Pain • Inflammation • Anxiety • Seizures • Sleep
Suggested effect:	• Analgesic • Antispasticity • Antinausea • Anti-inflammatory	• Analgesic • Neuroprotective • Anticonvulsant • Antioxidant

Interestingly, individual cannabinoids have different side effect profiles; the principle cannabinoids, CBD and THC, differ in the psychoactive effects exerted by THC.[13] While THC is psychoactive, co-administration of CBD with THC appears to reduce its psychoactive effects.[13,14] Also, the safety profile of CBD-containing preparations is wider than it is for THC-containing preparations, permitting greater exploration of dosing strategies.[14]

ACTIVE INGREDIENT EXTRACTION PROCESS

Cannabinoid extraction process, including CO^2 or ethanol, is used to collect the full spectrum crude oil containing 60% to 80% total cannabinoids depending on the nature and origin of the plant. The extracts contain cannabinoids, terpenes, flavonoids and other molecules such as pigments, sugars and fats. However, using crude oil as medication demonstrates some disadvantages including difficulties in titration for patients as well as unknown interactions with other natural compounds present in the extract. Therefore, purification of the crude oil, consisting of a controlled distillation process that fractionates crude extract into a more refined high cannabinoid content distillate, increases the purity and the potency up to 90%. This allows better control and quality of the dosage form for the patient. Further purification can be performed in order to isolate specific cannabinoids by crystallization, bringing the purity as high as classical pharmaceutical active ingredients (>99%). The active ingredients selected for RHO Phyto products include distillate and isolated cannabinoids.

POTENTIAL THERAPEUTIC USE OF MEDICAL CANNABIS

Medical cannabis has been used for a variety of therapeutic indications with a primary focus on symptom management.[4] Mounting evidence suggests the potential for treating symptoms of several conditions, including the following: [4]

Each of the above conditions often present with one or more condition(s) – known as comorbidities – such as anxiety, depression, appetite and sleep disturbances. Evidence has shown that medical cannabis can also help relieve comorbidities that are associated with health outcomes.[8,9]

CURRENT STATE OF EVIDENCE

Despite changing public attitudes on cannabis use and a shifting regulatory landscape, evidence regarding the short and long-term therapeutic benefits of cannabis remains scarce. In addition, there are currently no clinically accepted standards for dosing medical cannabis in specific therapeutic indications. The National Academies of Sciences, Engineering, and Medicines (NASEM) conducted a comprehensive review of the evidence for the therapeutic use of medical cannabis, summarized as follows:

Table 2. The level of evidence for medical cannabis in specific indications summarized by the NASEM. [5,15]

Level of evidence	Indication/Symptom
Conclusive/Substantial	• Chronic pain • Chemotherapy induced nausea and vomiting • Spasticity associated with Multiple sclerosis (MS)
Moderate Evidence	• Sleep disturbance (nabiximols)
Limited Evidence	• Appetite and weight gain associated with HIV/AIDS • Post-traumatic stress disorder (PTSD) • Anxiety • Tourette syndrome
Insufficient evidence to support or refute	• Cancer • Epilepsy* • Neurodegenerative disease (Huntington's disease, Parkinson's dyskinesia) • Irritable bowel syndrome (IBS) • Addiction

**There is now substantial evidence for childhood epilepsies based on clinical studies using a CBD pharmaceutical agent (Epidiolex®). [16]*

To date, two natural cannabinoid-based drugs have been licensed for pharmaceutical use:

1. Epidiolex®: oral CBD for use in childhood epilepsy, including Lennox-Gastaut or Dravet syndrome, in the United States and the European Union (EU).[16]
2. Sativex®: oromucosal spray with CBD and THC, for spasticity in Multiple Sclerosis and approved in many countries including the EU and Canada.[17]

PERSONALIZED CANNABINOID MEDICINE THROUGH HCP GUIDANCE

Under the current medical cannabis regulations, patients must speak with a HCP to discuss whether medical cannabis could be a useful alternative healthcare solution.[4] If it is determined that medical cannabis has the potential to provide a therapeutic effect then the HCP will provide a medical cannabis authorization form. Patients can then submit the form to a registered LP, such as Medical Cannabis by Shoppers to start purchasing products. Healthcare practitioners should work with their patients to define the most appropriate medical cannabis treatment program. As with any drug, HCP should advise their patients on potential adverse events and can suggest the use of a personal patient journal to monitor efficacy and side effects. Patients should also be informed about the type and concentration of cannabinoids in the preparation they are using and what they should expect. HCP should take into account the following considerations when defining personalized medical cannabis treatments:

Figure 5. The various factors that HCP must consider when developing a treatment plan for patients.

Note: It is particularly important to take into consideration any other medications being used by the patient, especially those affecting the cytochrome P450 hepatic enzyme system, either as inhibitors or inducers, as there may be potentially predictable clinical effects from increased or reduced serum drug concentrations. In this context, side effects may be erroneously attributed to the more recently introduced drug, in this case the cannabinoid, when in fact the toxicity or reduced efficacy is an effect of the previously prescribed agent (for more information on drug-drug interactions, see page 12).

Table 3. An overview of the risks that should be taken into consideration when prescribing medical cannabis. These considerations apply in particular to cannabinoid preparations containing THC and were adapted from the Canadian Health Care Professional Guideline.[4]

Risk	Description
Prescribing to those under 25 years of age	• The adolescent brain is still developing, therefore they may be more vulnerable to negative effects on brain structur and function. • Patients under the age of 25 are at greater risk for psychosocial harm related to cannabis use, including suicidal ideation, persistent psychosis, and illicit drug use.
Prescribing for older adults	• Older adult patients have an increased sensitivity to neurological and psychoactive effects of medical cannabis, particularly to that of THC, and can feel dizzy and lightheaded. This is evident in older adult patients with dementia and those who are prone to falls. • If considered appropriate and utilizing a medically supervised prescription, elderly patients should start at the low end of the dosing range.
Psychosis or other psychiatric conditions	• Cannabinoid preparations containing THC should not be used in patients with a family history or previous episodes of psychosis, psychiatric conditions or major depression.
Heart disease cardiac/ coronary conditions	• Cannabinoids can affect a patient's heart rate and blood pressure levels, which can cause cardiac ischemia. • Only under careful supervision by their HCP should patients consider using medicinal cannabis if they have a history of heart disease or are receiving heart medications.
Pregnancy and lactation	• Medical cannabis should not be prescribed prior to or during pregnancy as it could affect the development of the fetus. • Medical cannabis should not be used by patients who are breastfeeding.
Liver disease	• A high degree of caution should be placed on patients with liver disease, as they may have more difficulty metabolizing cannabinoids.
Addiction and anomalous prescribing	• Addiction to medical cannabis is not common. However, care should be taken if patients have prior history with problematic substance use. • Sudden treatment cessation may elicit withdrawal symptoms that can include restlessness, irritability, insomnia, vivid dreams, and decreased appetite.
Other medications	• Cannabis use can worsen the cognitive impairment caused by opioids, benzodiazepines, other sedatives, and alcohol.

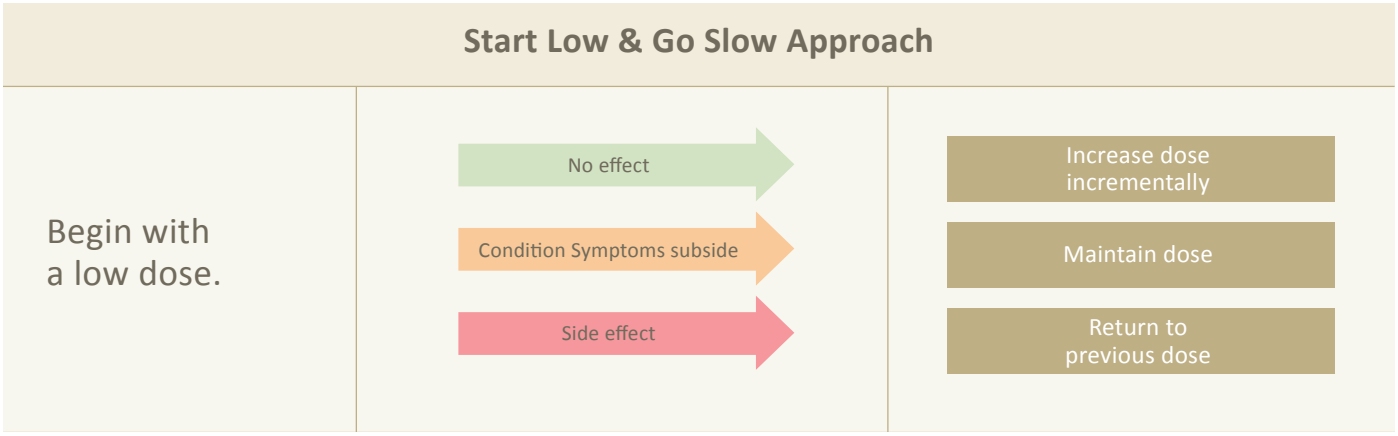
Note: for more information on the above, see Warnings and Precautions; Dependence, Tolerance, and Withdrawal Symptoms; and Potential Drug-Drug Interactions (Health Canada HCP Guidelines).[4]

It is essential that the prescribing HCP consider the risks associated with cannabinoid therapy in much the same way as they would another therapeutic agent, closely monitor patients with higher risk profiles and communicate regularly with any other HCP providing ongoing comprehensive care for the patient.

DOSAGE & TITRATION

In the absence of guidelines, it is recommended that HCP advise patients to take a "start low and go slow" approach in order to understand how their body reacts to cannabis. To achieve this, titration methods are used to find the right dose by which patients experience therapeutic effects with no or minimal adverse effects.

Figure 6. Guide to Start Low and Go Slow recommendations for prescribing medical cannabis. [14]



As everyone's response to medical cannabis may be different, patients should start with a low dose and discontinue use if they experience any adverse effects. However, the period of observation may be shorter or longer depending on the formulation and delivery method (for information regarding onset and duration of product forms, see Medical Delivery Forms, page 13). Treatment with cannabinoids should be both indication and product specific.

Table 4. Example of dosage form recommendations for acute and background anxiety.

Indication	**Anxiety**	
Components	*Acute*	*Background*
Recommendations	Fast-acting sublingual spray	Long-acting oral preparation

Careful titration permits a more precise determination of the lowest dose that achieves efficacy (e.g., seizure control), and therefore minimizes the risk of dose-dependent side effects. Titration also enables the prescriber to identify the most recent dose that was not associated with adverse effects and to return the patient to the previously prescribed lower dose, should the need arise.

If a patient does not experience the desired therapeutic effect(s) after a predetermined period, HCP may, depending on the individual context, try prescribing an alternative delivery form, or it may be recommended that use by the patient be discontinued.

POTENTIAL SIDE EFFECTS

If patients experience serious adverse events including major psychoactive effects, it is recommended to advise that product use be discontinued. Products that contain high amounts or concentrations of THC are more commonly associated with a higher risk of side effects.

Table 5. Side effects associated with cannabis-based medicines.[18]

Occurrence	*Most common*	*Common*	*Rare*
Side effects	Drowsiness, fatigue, dizziness, dry mouth, anxiety, nausea, cognitive effects	Euphoria, blurred vision, headache	Orthostatic hypotension, toxic psychosis or paranoia, depression, instability, tachycardia, cannabis hyperemesis, diarrhea

WARNINGS AND PRECAUTIONS

In addition to precautions taken with titration and dosing, HCP should consider the following general contraindications that have been set forth by Health Canada:[4]

- Prescription for anyone under the age of 25 with products high in THC
- Products high in THC for anyone with a previous or familial history of psychiatric conditions including schizophrenia, bipolar disorder, and psychosis
- Patients who have severe hepatic or renal disease, cardiovascular or cerebrovascular disease (i.e., at greater risk for hypertension, tachycardia, and stroke)
- Patients who are pregnant, planning to become pregnant, or breastfeeding
- Those who have a history of drug or substance disorders

WARNING: Patients should not drive or operate machinery after using medical cannabis as it may cause unwanted side effects such as dizziness and or drowsiness.

Note: Travelling outside of Canada with medical cannabis is illegal. For more information on international travel while carrying medical cannabis, please visit travel.gc.ca. If your patient is travelling with medical cannabis within Canada, ensure they ar prepared to show medical documentation. Their documentation and the amount of cannabis they carry must be in accordance with the Access to Cannabis for Medical Purposes Regulations.

For more in depth information, please consult "Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids" (Health Canada HCP Guidelines).[4]

DEPENDENCE, TOLERANCE AND WITHDRAWAL SYMPTOMS

Although cannabis is considered a "soft drug" with significantly lower risk of dependence than opioids or other psychoactive agents, it may lead to dependence, tolerance, and withdrawal symptoms following heavy or frequent use.[4,8] Cannabis dependency is divided into psychological and physical dependence and can occur particularly with chronic, heavy use, as outlined in the following chart below:

Table 6. Overview of the types of cannabis dependency that can occur with chronic use.

Cannabis Dependency Symptoms	
Psychological	***Physical***
Anxiety, aggression, depressed mood and/or irritability	Difficulty sleeping, stomach pain, headaches, appetite stimulation or suppression

Notably, the World Health Organization (WHO) Report on CBD states that CBD does not produce the same adverse effects caused by THC and is not associated with abuse potential.[19] Tolerance to cannabis results from mostly pharmacodynamic and pharmacokinetic mechanisms and can be followed by withdrawal symptoms.[4] Tolerance to most cannabis effects may occur following a few doses and can quickly dissipate following discontinuation of cannabis treatment.[4]

POTENTIAL DRUG-DRUG INTERACTIONS

The co-administration of medical cannabis products high in THC with central nervous system depressants (i.e., alcohol, barbiturates, and benzodiazepines) should be avoided.[4] Importantly, co-administration with stimulants such as cocaine, MDMA, and amphetamines can lead to increased risk of tachycardia. Additionally, co-administration with drugs that are broken down by isoenzymes CYP2C9, CYP2C19, CYP34A can lead to interactions that would act to increase the bioavailability of THC and lead to increased side effects. Examples of these drugs include macrolides, antimycotics, HIV protease inhibitors, anti-depressants (including tri-cyclic antidepressants), calcium antagonists, and proton pump inhibitors.[4] For a comprehensive list of potential drug-drug interactions, please see the Canadian Health Care Professional Guideline.

MEDICAL CANNABIS DELIVERY FORMS

As with any prescribed drugs, HCP and/or pharmacists should be involved in medical cannabis authorization and dosing. In addition to flower, medical cannabis products are available in various delivery forms, including sublingual sprays, oil drops, capsules, topical creams and gels. These varied delivery forms provide the HCP with several options in prescribing medical cannabis products that facilitate better dosing control and safer options in comparison to products that lack consistency, are of variable quality, or are smokable or inhalable.

Table 7. Properties of various medical cannabis delivery forms.[4,11,18]

Route of Administration	**Oral**		**Sublingual**	**Topical**
Product Type	***Oil Drops***	***Capsules***	***Sublingual Spray***	***Creams, Gels***
Pros of Delivery Form	Ability to titrate, less odor, convenient, and discreet	Predetermined dosage, common delivery form	Faster onset compared to medium chain triglyceride oil. Convenient and discreet	Ideal for local or deep tissue delivery, less systematic effect

MEDICAL CANNABIS AND RHO PHYTO BY AVICANNA

RHO Phyto's unique formulations have undergone extensive research and development to create a line of products that meet the quality and consistency standards that patients and physicians should expect of medical cannabis products. The RHO Phyto line consists of advanced oral and topical delivery forms of medical cannabis extracts including oil drops, sublingual sprays, soft-gel capsules, and topical creams and gels. All RHO Phyto formulations are designed to maintain

Why is product stability important?

Cannabinoids that are extracted from the cannabis plant tend to degrade over a short period of time resulting in a product that may not have the same efficacy over time. Currently, there are no requirements for testing product stability. As a result, patients could be taking doses containing less mg of CBD or THC than written on the label.

the stability of the cannabinoids to ensure more consistent clinical effects over the course of treatment. These formulations are optimized for increased and faster absorption of cannabinoids relative to basic MCT (medium-chain triglyceride) oil formulations. All RHO Phyto products are made under Good Manufacturing Practices (GMP) with adherence to strict standards for pharmaceutical quality.

Figure 7. RHO Phyto medical cannabis products come in various delivery forms.

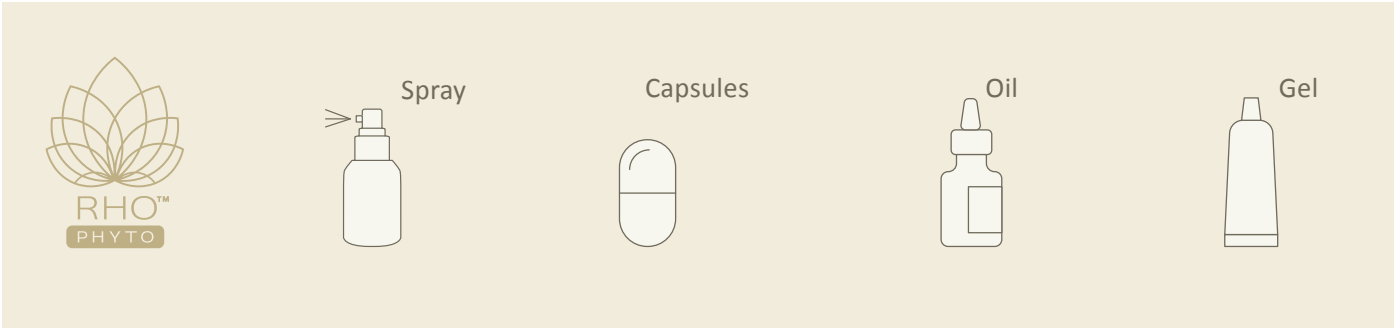


Table 8. RHO Phyto products are developed using Avicanna's quality standards as outlined below:

AQ AVICANNA STANDARD OF QUALITY	*Accuracy of Dosing*	*Bioavailability*	*Onset of Action*	*Stability*	*Reproducibility*	*Drug Delivery*
Definition	How close the dosing unit is to the intended dose	The percentage of the dose absorbed into the bloodstream	Duration of time for the effects of a product to become apparent	A product's ability to maintain its physical and chemical properties and concentration of cannabinoids over time	Degree to which the same drug and formulation properties are achieved time after time	The dosage form and route of administration by which a product can achieve its desired therapeutic effect
RHO Phyto by Avicanna	Standardized methods to provide accurate cannabinoid concentrations	Advanced formulations to increase absorption backed by preclinical studies	Optimized formulations for faster onset versus basic MCT (medium-chain triglyceride) oil	Formulations tested to ensure the stability of cannabinoids for extended periods of time	Standardized operating and quality assurance procedures	Products delivered via oral, sublingual and topical methods

SUGGESTED RECOMMENDATIONS FOR USING CANNABINOIDS

HCP may recommend cannabinoid-based products to treat a wide variety of conditions as listed in the section titled Current State of Evidence (page 7). As mentioned, a comprehensive review of the evidence finds support for its use for conditions such as epilepsy, MS, anxiety, depression, insomnia, and some types of chronic pain.[5,15] Often, primary medical conditions, particularly neurological disorders such as epilepsy and MS, are accompanied by secondary comorbidities, such as anxiety, depression and insomnia. Thus, treatment of the primary conditions using cannabinoids may have additional benefits due to their effect on associated comorbidities.

While anxiety, depression and sleep disorders may occur on their own as primary conditions without an underlying medical disorder, these conditions are extremely heterogenous in aetiology and as such, precise guidelines cannot be provided. Instead, it is left to the discretion of the HCP to recommend a product based on individual patient characteristics and a dosage again determined through careful titration.

It should also be noted that some conditions including chronic pain and MS can have intermittent, sometimes abrupt increases in the severity of symptoms including pain and MS-related spasticity. For abrupt increases in symptoms, faster-acting sublingual sprays, provide the opportunity for quicker relief.

Table 9. Examples of product selection options for selected medical conditions.

CBD ONLY	HIGH IN CBD LOW IN THC	MODERATE CBD LOW THC	BALANCED CBD AND THC
CBD ONLY	**LOW RATIO THC:CBD (1:25)**	**MODERATE RATIO THC:CBD (1:4)**	**HIGH RATIO THC:CBD (1:2)**
- Severe Childhood Epilepsies (e.g. Dravet and Lennox Gastaut Syndromes)[16] - Anxiety[21, 26] - Inflammation[21, 29]	- Severe Childhood Epilepsies (e.g. Dravet and Lennox Gastaut Syndromes)[16] - Anxiety[21, 26] - Pain[21] - PTSD[25] - Inflammation[22, 29]	- Pain[21] - Multiple Sclerosis related Spasticity[17,27,28] - Sleep[23]	- Pain[21] - Sleep[23,26] - Cancer induced Nausea & Vomiting[24]

Note: These recommendations are based on anecdotal and limited scientific data. These should not be considered therapeutic claims. Other product options may benefit individual patients with the same conditions. Cannabis is not an approved drug in Canada and its efficacy in treating conditions at any dose has not been established. For more information on each therapeutic indication, please consult the Health Canada Health Care Professional Guideline.[4]

Table 10. RHO Phyto product range cannabinoid ratios and the rate of relief.

THC:CBD RATIOS	CBD only		1:25	1:20	1:4	1:2	15:1	
RHO Phyto Product	Micro Drop 50 CBD	Rapid Act Spray 40 CBD	Micro Drop 2:50 CBD	Rapid Act Spray 2:40 CBD	Micro Drop 5:20 CBD	Rapid Act Spray 10:20 CBD	Micro Drop 15:1 CBD	Rapid Act Spray 15:1 CBD
Rate of Relief	Slow	Faster	Slow	Faster	Slow	Faster	Slow	Faster

AUTHORIZING MEDICAL CANNABIS USE

Step 1: Prescribe Medical Cannabis

Advise your patients on which medical cannabis treatment is right for them. Remind patients to start low & go slow and provide direction on increasing or decreasing dosage levels.

Step 2: Complete a Medical Document for your patient

Fill out a medical document form for your patient. Your patient will either bring you a form or you can download a copy here:

Option 1

Medical Cannabis by Shoppers
Online Portal
https://cannabis.shoppersdrugmart.ca/en_CA/downloads

Submitting Documents

By secure fax
1-866-220-2627

By mail
Medical Cannabis by Shoppers
6941 Kennedy Road, Unit 100
Mississauga, ON L5T 2R6

Option 2

My Cannabis Clinic
Refer your patient to an online clinic
https://mycannabisclinic.org/medical-form/

Step 3: Make sure your patient is registered with Medical Cannabis by Shoppers

Your patient will need to register with Medical Cannabis by Shoppers before they can order medical cannabis. Registration processing time can take up to 48 hours once the Medical Document and Registration Form are received. Medical Cannabis by Shoppers will reach out to your patient once they have finalized registration.

Step 4: Schedule check-ins with your patient as needed

Be sure to check-in with your patient one month after initial prescription and as needed over the course of their treatment. Please note that medical documents are only valid for 1 year.

ABOUT AVICANNA INC.

Avicanna is a Canadian biopharmaceutical company providing advanced cannabinoid solutions through an evidence-based approach. As a multinational organization with vertical integration, Avicanna is focused on utilizing scientific research related to plant-derived cannabinoid products through its internal research platforms, real-world evidence trials, and strategic collaborations with world-class research institutions.

Avicanna's research and development is conducted at its Canadian headquarters within the Johnson & Johnson Innovation Centre JLABS @ Toronto located in the MaRS Discovery District. Avicanna's RHO Phyto formulations are scientifically optimized and studied in collaboration with the Christine Allen Research Group (CARG) at the Leslie Dan Faculty of Pharmacy of the University of Toronto, a leading research laboratory for pharmaceutical development in Canada. Avicanna's partnership with CARG has been focused on formulation optimization, and preclinical characterization of the RHO Phyto products which includes stability, drug release and safety studies.

Avicanna is committed to providing an unparalleled quality of natural cannabinoid solutions that foster informed communities and improve quality of life.

AVICANNA'S CLINICAL RESEARCH PROGRAM

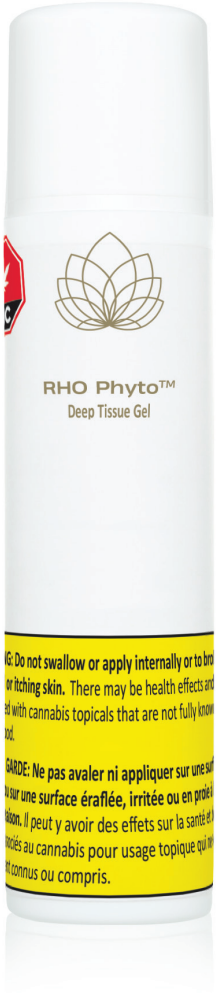
Avicanna's research and development activities over the past 4 years have been focused on the development, optimization and clinical evaluation of cannabinoid product types ranging from consumer derma-cosmetics, medical cannabis (such as the RHO Phyto product line) and pharmaceutical products. Avicanna has commercialized several of these products after conducting rigorous research and development. The Company's clinical research program is focused on building the medical evidence for advanced cannabinoid products to address specific health conditions and their comorbidities. Furthermore, Avicanna is committed to further developing and optimizing cannabinoid formulations to create products that will better address patient needs.

Avicanna has partnered with leading Canadian universities and research hospitals for R&D and clinical trials on the formulations underlying its RHO Phyto product line. Among these world class collaborations are the University of Toronto, University of Guelph, Toronto's Hospital for Sick Children (SickKids) and other leading Canadian institutions.

Avicanna is currently planning a number of clinical trials, from observatory to Phase II randomized, double blind, placebo-controlled studies, using the RHO Phyto products at Toronto's leading research hospitals. More information will be available following Health Canada approvals.

RHO PHYTO PRODUCT OFFERINGS

RHO™
PHYTO



Deep Tissue
Gel

Rapid Act
Spray

Micro Drop
Oil

RHO PHYTO MICRO DROP OILS (30 ML)

RHO Phyto's Micro Drops are offered in a blood orange flavour and deliver metered dosing for easy titration. As a result of years of research and development, these advanced formulations are designed to provide higher and faster cannabinoid absorption compared to basic MCT (medum-chain triglyceride) oil products available in the market. RHO Phyto's unique combination of ingredients helps maintain the stability of the cannabinoids to ensure more consistent dosing over the course of treatment. Developed with the patient in mind, these products allow for discreet self-administration.

Micro Drop Oil is also available in a tetrahydrocannabinol (THC)-Free formula. It is designed to limit side-effects commonly associated with THC and provide an alternative for users that would like to avoid products containing THC.

HOW TO USE

Shake the bottle well before using to ensure the extract is evenly mixed with the oil. Hold bottle upside down and drop the dose amount onto your tongue and swallow. Alternatively, you can count out the number of oil drops on a spoon to ensure accurate dosing.

Product Name	Ratio	Per Drop		mg per mL		Per bottle		Active Ingredient
	THC:CBD	*THC*	*CBD*	*THC*	*CBD*	*THC*	*CBD*	
Micro Drop 2:50 CBD	1:25	0.06 mg	1.6 mg	2 mg	50 mg	60 mg	1500 mg	CBD Distillate
Micro Drop 5:20 CBD	1:4	0.16 mg	0.6 mg	5 mg	20 mg	150 mg	600 mg	CBD & THC Distillate
Micro Drop 50 CBD	0:50	0 mg	1.6 mg	0 mg	50 mg	0 mg	1500 mg	Purified CBD THC FREE

Legend: Advanced · High absorption · Faster onset · Cooling effect · Fast acting

CONVERSION TABLE | MICRO DROP 2:50 CBD

# of drops	1 drop	8 drops	16 drops	24 drops	32 drops
	0.03 mL	0.25 mL	0.5 mL	0.75 mL	1 mL
THC	0.1 mg	0.5 mg	1 mg	1.5 mg	2 mg
CBD	1.6 mg	12.5 mg	25 mg	37.5 mg	50 mg

DOSING GUIDE

Day one: Start with 3 drops or 0.09 mL (i.e. 0.2 mg THC and 4.7 mg CBD) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 3 drops or 0.09 mL (i.e. 0.2 mg THC and 4.7 mg CBD) orally early in the evening until you reach an effective dose. If you begin to feel side effects then you should lower the dose to the previous dose and re-assess with your healthcare provider.

Days seven and onwards: Once you have established an effective dose without experiencing side effects then consider repeating the same dose 2 to 3 times per day.

CONVERSION TABLE | MICRO DROP 5:20 CBD

# of drops	1 drop	8 drops	16 drops	24 drops	32 drops
	0.03 mL	0.25 mL	0.5 mL	0.75 mL	1 mL
THC	0.16 mg	1.25 mg	2.50 mg	3.75 mg	5 mg
CBD	0.6 mg	5 mg	10 mg	15 mg	20 mg

DOSING GUIDE

Day one: Start with 3 drops or 0.09 mL (i.e. 0.5 mg THC and 1.9 mg CBD) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 3 drops or 0.09 mL (i.e. 0.5 mg THC and 1.9 mg CBD) orally early in the evening until you reach an effective dose. If you begin to feel side effects then you should lower the dose to the previous dose and re-assess with your healthcare provider.

Days seven and onwards: Once you have established an effective dose without experiencing side effects then consider repeating the same dose 2 to 3 times per day.

Please note that cannabis naïve patients, older individuals and other susceptible clinical populations may experience significant THC-related side-effects even at low doses.

CONVERSION TABLE | MICRO DROP 50 CBD

mL	0.1 mL	0.5 mL	1 mL
CBD	5 mg	25 mg	50 mg

THC FREE

Metered dosing on syringe

HOW TO USE

Press syringe into bottle adapter at the top of the bottle. Once secure, turn the bottle upside down and gently pull on plunger of syringe to dispense desired amount of oil. When you have dispensed the correct dose, flip the bottle right side up and remove syringe from top of bottle.

DOSING GUIDE

Day one: Start with 0.1 mL (5 mg CBD) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 0.1 mL (i.e. 5 mg CBD) orally early in the evening until you reach an effective dose. If you begin to feel side effects then you should lower the dose to the previous dose and re-assess with your healthcare provider.

Days seven and onwards: Once you have established an effective dose without experiencing side effects then consider repeating the same dose 2 to 3 times per day.

RHO PHYTO RAPID ACT SPRAYS (15 ML)

RHO Phyto's Rapid Act Sprays offered in lemon-mint flavour, are administered under the tongue to provide more direct absorption into the bloodstream by avoiding first pass metabolism by the gut and liver. RHO Phyto's Rapid Act Sprays are optimized for increased absorption and faster onset in comparison to basic MCT (medium-chain triglyceride) sublingual sprays. Rapid Act Sprays are discreet, easy to use, and convenient.

Rapid Act Spray is also available in a tetrahydrocannabinol (THC)-Free formula. It is designed to limit side-effects commonly associated with THC and provide an alternative for users that would like to avoid products containing THC.

HOW TO USE

Shake the bottle well before using. Place nozzle under the tongue and push down on the pump to spray. For maximum absorption hold spray under tongue for 30-90 seconds before swallowing.

Product Name	Ratio	Per Drop		mg per mL		Per bottle		Active Ingredient
	THC:CBD	*THC*	*CBD*	*THC*	*CBD*	*THC*	*CBD*	
Rapid Act Spray 2:40 CBD	1:20	0.2 mg	4 mg	2 mg	40 mg	30 mg	60 mg	CBD Distillate
Rapid Act Spray 10:20 CBD	1:2	1 mg	2 mg	10 mg	20 mg	150 mg	300 mg	CBD & THC Distillate
Rapid Act Spray 15:1 CBD	15:1	1.5 mg	0.1 mg	15 mg	1 mg	225 mg	15 mg	THC Distillate
Rapid Act Spray 40 CBD	0:40	0 mg	4 mg	0 mg	40 mg	0 mg	600 mg	Purified CBD THC FREE

Legend: Advanced · High absorption · Faster onset · Cooling effect · Fast acting

CONVERSION TABLE | RAPID ACT SPRAY 2:40 CBD

# of sprays	1 spray	5 sprays	10 sprays
	0.1 mL	0.5 mL	1 mL
THC	0.2 mg	1 mg	2 mg
CBD	4.0 mg	20.0 mg	40.0 mg

1 spray is equivalent to 0.1 mL

DOSING GUIDE

Day one: Start with 1 spray under the tongue (i.e. 0.1 mL = 0.2 mg THC and 4 mg CBD) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 1 spray (i.e. 0.1 mL = 0.2 mg THC and 4 mg CBD) orally early in the evening until you reach an effective dose. If you begin to feel side effects then you should lower the dose to the previous dose and re-assess with your healthcare provider.

Days seven and onwards: Once you have established an effective dose without experiencing side effects then consider repeating the same dose 2 to 3 times per day depending on individual duration of action.

CONVERSION TABLE | RAPID ACT SPRAY 10:20 CBD

# of sprays	1 spray	5 sprays	10 sprays
	0.1 mL	0.5 mL	1 mL
THC	1 mg	5 mg	10 mg
CBD	2 mg	10 mg	20 mg

1 spray is equivalent to 0.1 mL

DOSING GUIDE

Day one: Start with 1 spray under the tongue (i.e. 0.1 mL = 1 mg THC and 2 mg CBD) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 1 spray (i.e. 0.1 mL = 1 mg THC orally and 2 mg CBD) early in the evening until you reach an effective dose. If you begin to feel side effects, then you should lower the dose to the previous dose and re-assess with your healthcare provider.

Days seven and onwards: Once you have established an effective dose without experiencing side effects then consider repeating the same dose 2 to 3 times per day depending on individual duration of action.

Please note that cannabis naïve patients, older individuals and other susceptible clinical populations may experience significant THC-relate side-effects even at low doses.

CONVERSION TABLE | RAPID ACT SPRAY 15:1 CBD

# of sprays	1 spray	5 sprays	10 sprays
	0.1 mL	0.5 mL	1 mL
THC	0.1 mg	0.5 mg	1 mg
CBD	1.5 mg	7.5 mg	15 mg

1 spray is equivalent to 0.1 mL

DOSING GUIDE

Day one: Start with 1 spray under the tongue (i.e. 0.1 mL = 1.5 mg THC and 1 mg CBD) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 1 spray (i.e. 0.1 mL = 1.5 mg THC and 1 mg CBD) orally early in the evening until you reach an effective dose. If you begin to feel side effects then you should lower the dose to the previous dose and re-assess with your healthcare provider.

Days seven and onwards: Once you have established an effective dose without experiencing side effects then consider repeating the same dose 2 to 3 times per day depending on individual duration of action.

CONVERSION TABLE | RAPID ACT SPRAY 40 CBD

# of sprays	1 spray	5 sprays	10 sprays
	0.1 mL	0.5 mL	1 mL
CBD	2 mg	10 mg	20 mg

1 spray is equivalent to 0.1 mL

DOSING GUIDE

Day one: Start with 1 spray under the tongue (i.e. 0.1 mL = 4 mg CBD) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 1 spray (i.e. 0.1 mL = 4 mg CBD) orally early in the evening until you reach an effective dose. If you begin to feel side effects then you should lower the dose to the previous dose and re-assess with your healthcare provider.

Days seven and onwards: Once you have established an effective dose without experiencing side effects then consider repeating the same dose 2 to 3 times per day depending on individual duration of action.

Please note that cannabis naïve patients, older individuals and other susceptible clinical populations may experience significant THC-relate side-effects even at low doses.

RHO PHYTO DEEP TISSUE GEL (50 ML)

RHO Phyto Deep Tissue Gel combines unique ingredients and natural polyphenols in an advanced emulsion formulation to consistently deliver the same amount of CBD in every pump. Years of research and development have optimized this formulation for improved stability and faster absorption of cannabinoids into the deeper layers of the skin. RHO Phyto's Deep Tissue Gel is stored in pharmaceutical grade airless packaging, which provides protection from light and air to preserve the integrity of the product. This quick absorbing gel comes in a mint scent and delivers a cooling effect.

HOW TO USE

Apply gel on sore spots and massage into the skin until gel is completely absorbed. For topical use only.

DOSE

Apply gel to affected area two to three times a day.

Product Name	Ratio	mg per 1 mL		Per 50 mL bottle		Active Ingredient
	THC:CBD	*THC*	*CBD*	*THC*	*CBD*	
Extra Strength Deep Tissue Gel	1:25	0.2 mg	5 mg	10 mg	250 mg	CBD Distillate
Regular Deep Tissue Gel	2:25	0.2 mg	2.5 mg	10 mg	125 mg	CBD Distillate

Legend: Advanced · High absorption · Faster onset · Cooling effect · Fast acting

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