MyMedi.ca

MEDICAL CANNABIS CARE

Health Care Practitioners

PHONE
1-844-500-2040 (Toll-Free)

FOR ALL PATIENT AND HEALTHCARE PROVIDER INQUIRIES
support@mymedi.ca

SECURE FAX FOR MEDICAL DOCUMENT
1-844-500-4042 (Main)
289-499-3791 (Alternative)

WEBSITE
mymedi.ca

MAILING ADDRESS
MyMedi.ca c/o Northern Green Canada Inc.
1-275 Orenda Road, Brampton
ON L6T 3T7

LICENCE INFORMATION
Licence Number: LIC-NS4TE0CY1U-2021

LINK TO DOCUMENTS FOR DOWNLOAD
http://www.mymedi.ca/patient/

This guide is intended to provide you with information to make informed decisions about how to incorporate medical cannabis into medical practice. It covers administration, dosing and titration guidance, potential side effects, warnings and precautions, and how to recommend particular products. The purpose of this document is to provide medical information and not to serve as 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 judgment of healthcare practitioners.

The information contained in this guide is provided 'as-is' and without any warranties of any kind, whether expressed or implied, including but not limited to, implied satisfaction, quality, fitness for a particular purpose and/or correctness.

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ABOUT MYMEDI.CA

MyMedi.ca is a medical cannabis care platform formed through an alliance between the medical community, patients and industry partners to better serve patients' needs.

MyMedi.ca's medical cannabis care platform is formed with the aim to better serve medical cannabis patients' needs and enhance the patient journey. MyMedi.ca launched in August 2023 and features diverse and scientifically curated products from leading Canadian licensed producers in addition to pharmacist-led patient support programs and educational resources to facilitate the incorporation of medical cannabis into health care regimens.

We also provide specialty services to distinct patient groups such as veterans and collaborate with public and private insurers to provide online or manual direct billing for patients with medical cannabis coverage.

KEY HIGHLIGHTS

- **Pharmacist-led consultations** and personalized treatment plan support
- **Dedicated patient support team** offering education, product selection guidance, ordering assistance, and issue resolution
- **Discount programs** available for seniors, pediatric patients, first responders, actively-serving military members and their spouses, as well as compassionate pricing options
- **Specialized programs** tailored to support Veterans
- **Direct billing and insurance support**, including preferred vendor arrangements for WSIB and WSBC
- **Assistance with motor vehicle accident claim processing**
- **Eligibility for medical tax deductions** and coverage through health spending accounts
- **High product quality standards** and strict freshness policies

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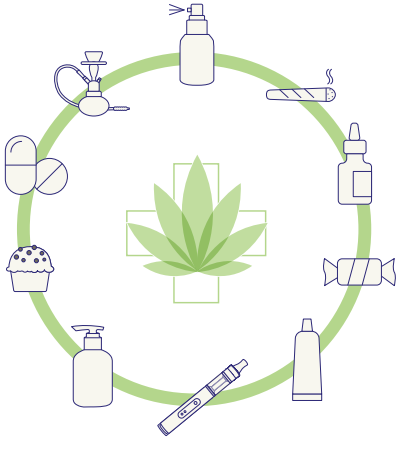
MEDICAL CANNABIS CARE

NORTHERN GREEN CANADA

BRIEF HISTORY OF CANNABIS

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. Consequently, 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

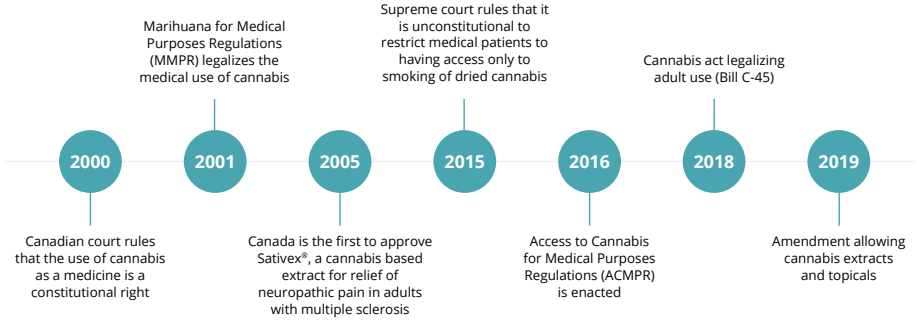


Despite this, in the ensuing years, studies were performed using whole plant extracts, cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC) isolates as treatments.[2, 3] Unfortunately, most of these studies were limited by a number of methodological problems including being underpowered, poorly designed, 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] More recently, a 2018 review of cannabidiol by the World Health Organization (WHO) concluded that CBD does not appear to have abuse potential, cause harm or public health problems, therefore recommending that CBD should no longer be internationally scheduled as a controlled substance.[1]

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.[5] Patients demanded access to legal medical cannabis and on July 30, 2001, the Marihuana Medical Access Regulations (MMAR) were 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 17, 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[5]

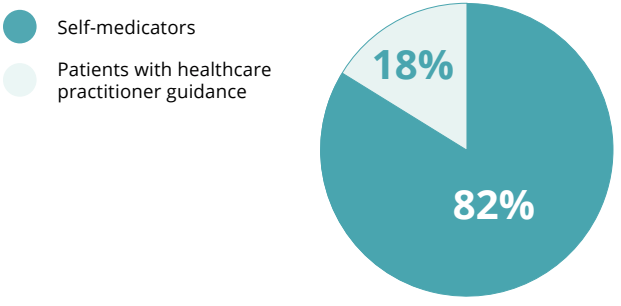


MEDICAL CANNABIS USE IN CANADA & HARM REDUCTION

Currently, there are over 200,000 patients registered to use cannabis for medical purposes.[6] Yet, the Canadian Cannabis Survey 2023 reported that 82% of medical cannabis users are self-medicating without the guidance of healthcare practitioners (HCP).[7] This is in contrast to a 2019 report from the Canadian Pharmacists Association that found that only 61% of medical cannabis users were self-medicating.[8] Unfortunately, many of these patients end up seeking advice from budtenders, family & friends, and online resources to make choices around their medical cannabis regimens, putting them at risk for choosing products that could exacerbate their medical conditions, cause unintended side effects or interact with their prescription medications.[7] Therefore, it is critical to create an open dialogue with patients about medical cannabis to help mitigate these risks.

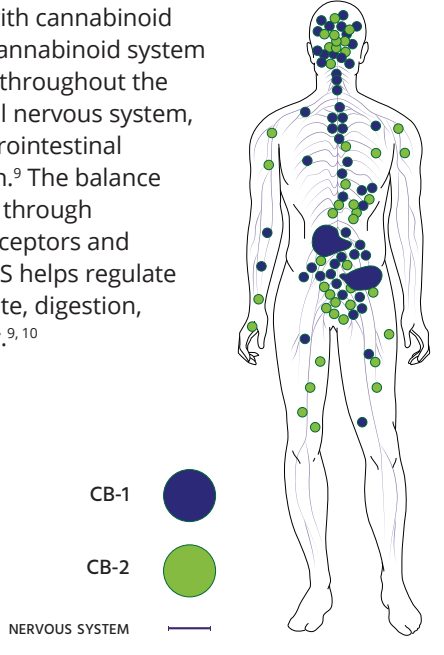
Prior to January 2020, the medical products available for patients were extremely limited, with product offerings consisting mainly of dried flower and basic oil drops. However, novel delivery forms and more advanced formulations can provide patients with alternatives that reduce risk to the lungs and optimize the pharmacokinetics profile of cannabinoids. Additionally, over 75% of patients prefer smokeless and non-inhalation product alternatives for medical use.[7]

Figure 3. A 2023 Canadian Cannabis Survey evaluated how many users of cannabis for medical purposes did so with the support of a HCP[7]



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]



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, a partial agonist of the CB1 receptor, is known for its psychoactive effect or "high" sensation that alters mood or mental state. In contrast, CBD, a negative allosteric modulator of the CB1 receptor, is non-psychoactive, meaning it does not produce a "high" feeling.[13] To note, cannabinoids have also been shown to interact with various molecular targets including but not limited to serotonergic (5-HT1A), transient receptor potential vanilloid subtype (TRPV1), dopaminergic (D2), G protein-coupled receptor-55 (GPR55), and μ-opioid receptors (MOR).[9] The wide range of pharmacological actions continue to be studied across various indications and for their role in symptom management.[14]

Table 1. Overview of the benefits of THC and CBD[15, 22]

	THC	CBD
Shown to Be Effective With	• 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 with CBD appears to reduce its psychoactive effects, generally improving tolerability.[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]

More recently, other minor cannabinoids such as cannabigerol (CBG) and cannabinol (CBN) have been identified for their potential therapeutic benefits.[16] In contrast with THC and CBD, it is important to note that most evidence for the therapeutic effects of these minor cannabinoids comes mainly from preclinical studies. CBG has been reported to act as a weak partial agonist for both CB1 and CB2, and is considered non-psychoactive.[16] In addition, CBG has been shown to modulate adrenergic, 5-HT1A, Peroxisome Proliferator-Activated (PPAR) Receptors, TRP channels, and Cyclooxygenase (COX) enzymatic activity.[17] CBN is an agonist at both cannabinoid receptors and modulates TRP channels.[18] However, CBN binds to CB1 receptors with 10 times lower affinity than THC and is generally considered relatively non-psychoactive.[18] Table 2 highlights the potential efficacy of CBG and CBN.

Table 2. Potential benefits of CBG and CBN[16-21]

	Cannabigerol (CBG)	Cannabinol (CBN)
Potential Therapeutic Effects	• Pain and/or inflammatory related indications • CBG + CBD: local analgesic and anti-inflammatory effects • Anxiety and neurological disorders	• Sleep disorders • Analgesia, and anti-inflammatory • Appetite stimulating

CANNABINOID EXTRACTS USED IN PRODUCTS

It is important to understand that not all cannabinoid-based non-inhalable products are made with the same level of cannabinoid purity. The extract used as input to develop products can impact patient outcomes. There are three main extract categories that are used in non-inhalable products, which are defined in Table 3 below. The most common type of extract used in product is full or broad-spectrum oil, which requires the least extensive processing and manufacturing requirements.

ⓘ ***COMMON TERMINOLOGY***

Full spectrum CBD has naturally occurring cannabinoids, terpenes, and up to 0.3% THC, while broad spectrum CBD also contains cannabinoids, and terpenes but with a non-detectable level of THC.

Table 3. Types and level of purity in cannabinoid-based extracts

Extraction Categorization	Cannabinoids Purity	Other Constituents	Critical Consideration
Full or Broad-Spectrum Oil	60-80% cannabinoids	20-40% of terpenes, flavonoids, and other molecules such as pigments, sugars and fats	Can lead to inconsistency in product effects due to ranges in purity and impact of other constituents
Distillate	85-95% cannabinoids	5-15% terpenes, flavonoids and other molecules such as pigments, sugars and fats	More controlled than full spectrum; higher quality dosage form
Isolate (Crystallization)	>99% purity	<1%	Controlled outcome and consistent dosing; purity consistent with Active Pharmaceutical Ingredient specifications (>99%)

ⓘ ***DID YOU KNOW?***

There are cannabis products that contain less than 0.01µg of THC. These types of products are considered THC-free. Products that qualify for this are not required to have the THC warning sign. If you would like to ensure that patients do not take THC then choose products that are "THC-free" and do not contain the THC warning sign.

POTENTIAL THERAPEUTIC USE OF MEDICAL CANNABIS

Medical cannabis has been used for a variety of therapeutic indications with a primary focus on symptom management including pain, sleep disruptions, low appetite, anxiety and/or mood related disruptions.[4, 8, 9] Mounting evidence suggests the potential for treating symptoms of several conditions, including the following:

Figure 4. Suggested uses of cannabis for medical purposes based on level of evidence[4]

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 in Table 4.[22]

Table 4. The level of evidence for medical cannabis use for specific indications summarized by NASEM[15, 22-24]

Level of Evidence	Indication/Symptom
Conclusive/Substantial	• Chronic pain • Spasticity related to multiple sclerosis • Chemotherapy-induced nausea and vomiting • Refractory epilepsy (Lennox-gastaut and Dravet syndromes)*
Moderate	• Sleep disorders related to chronic medical conditions (Chronic pain, multiple sclerosis, fibromyalgia, obstructive sleep apnea OSA) • High intraocular pressure due to glaucoma
Limited	• Dementia • Schizophrenia • PTSD • Appetite disorders and weight loss related to HIV/AIDS • Parkinson's disease • Social Anxiety Disorder (CBD)
Insufficient Evidence to Support or Refute	• Depression related to chronic pain and/or multiple sclerosis • Addiction • Inflammatory bowel disease • Amyotrophic lateral sclerosis • Huntington's diseases

*There is now substantial evidence for childhood epilepsies based on clinical studies using a CBD pharmaceutical agent (Epidiolex®)[25]

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, the European Union (EU), and Canada.[25]
2. Sativex®: Oromucosal spray with CBD and THC, for spasticity in multiple sclerosis and approved in many countries including the European Union (EU) and Canada.[26]

PERSONALIZED CANNABINOID MEDICINE THROUGH HCP GUIDANCE

Under the current medical cannabis regulations, patients must speak with an 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 safely provide a therapeutic effect, then the HCP will provide a medical cannabis authorization form. Patients can then submit the form to a registered Licensed Producer (LP), to start purchasing products from their authorized medical cannabis portals such as MyMedi.ca. Healthcare practitioners should work with their patients to define the most appropriate medical cannabis treatment program. As with any drug, an 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. The HCP should take into account the following considerations when defining personalized medical cannabis treatments:

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

NOTE TO PRACTITIONERS

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 16).

Table 5. 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 structure 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 patients 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 in particular pertaining to CBD.
Addiction Andanomalous 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 TO PRACTITIONERS***

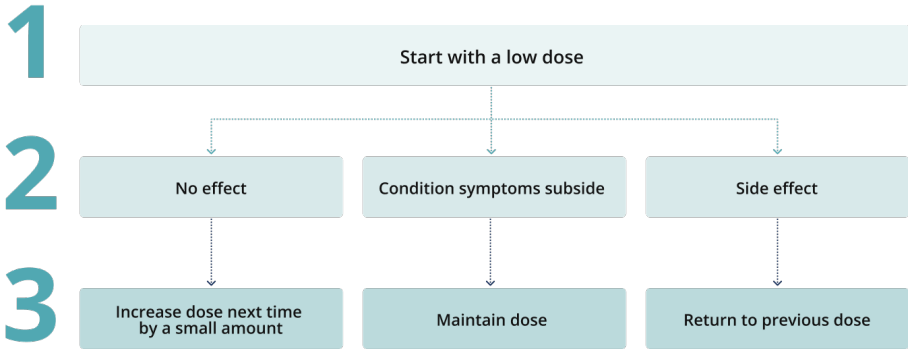
For more information on the above, see Warnings and Precautions; Dependence, Tolerance, and Withdrawal Symptoms (page 15); and Potential Drug-Drug Interactions (page 16 and Health Canada HCP Guidelines).[4]

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 monitoring patients with higher risk profiles and communicating regularly with any other HCP providing ongoing comprehensive care for the patient. Drug-drug interactions are extremely relevant and should be assessed before, during and at the end of treatment with medical cannabis. For more information on drug-drug interactions, please go to page 16 of HCP guideline.

DOSAGE & TITRATION

In the absence of guidelines, it is recommended that the 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[23]



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 on page 17). Treatment with cannabinoids should be both indication and product specific.

Table 6. 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, the HCP may, depending on the individual context, try prescribing an alternative delivery form or cannabinoid ratio.

RECENT DOSING AND TITRATION GUIDELINES

In recent years, there have been several guidelines published for healthcare professionals aimed at providing guidance around medical cannabis use in a variety of patient populations. Table 6 summarizes key information from some of the most recent guidelines, which act as useful references for prescribers. Please note that this list is not exhaustive. Table 7 outlines detailed consensus-based recommendations on dosing in patients suffering from chronic pain (neuropathic, inflammatory, nociceptive and mixed).[27] This guideline prioritizes safety and details what experienced prescribers have seen to be effective in their practice and can be a useful tool in developing oral dosing regimes with patients.

Table 7. List of recent clinical references listed by area of interest

Area	Methods & Aims	Key Highlights or Recommendations
Clinical Guideline: Chronic Pain & Comorbidities[28]	• Systematic review of 70 studies (19 systematic reviews and 51 original research studies) investigating the use of CBM for the treatment of chronic pain and comorbidities • GRADE system rates strength of recommendations and quality of evidence	**Recommendations:** • Use as adjunct treatment (monotherapy or replacement) when not achieving adequate response **Strong grading:** • Central and/or peripheral neuropathic pain, HIV related symptoms, MS, arthritic conditions, fibromyalgia, appetite loss, anxiety, unsatisfactory analgesia from opioid, or opioid sparing **Weak grading:** • Chronic migraine or headache, nausea, PTSD symptoms, depression
Consensus Recommendations: Chronic Pain[29]	• Consensus recommendations based on a multi-stage, modified Delphi process dosing protocols based on experience	**Recommendations:** • Use inhaled formats for breakthrough pain only • Follow up 2-4 weeks until stable dosing • Drug-drug interactions outlined
Canadian Pediatric Society Position Statement on Medical Cannabis:[30]	• Therapeutic considerations should be condition-specific, based on available data, include a clear treatment, following slow titration and follow-up plan GRADE system rates strength of recommendations and quality of evidence • Lennox-Gastaut & Dravet Syndrome (DRE) using purified CBD with a 36-46% reduction of seizure frequency. And dose tolerability up to 25mg/kg • Autism: positive effects of CBD in behavioral, anxiety, and core autism symptoms with mild adverse effects • Other conditions: cerebral palsy, TBI), cancer and palliative care	**Highlights:** • Indication, dosing regimen & report adverse events from clinical trails • CBD-enriched extracts show comparable safety/ efficacy to purified CBD in various conditions lower doses • Engage in evidence-based and unbiased discussion around the benefits & risks, to make informed decisions around medical cannabis as a treatment option • Strength based on risk and benefits
Sleep-Related Disorders:[31, 32]	**PTSD treatment resistant nightmares:** • PTSD Nightmare: n= 47 • Patients self-reported severity of nightmares and time asleep • 0.2mg-4mg of nabilone **Insomnia:** • Double-blind prospective (n=1793) • Sleep disturbance was assessed at baseline and at 4 weeks • Patient-Reported Outcomes Measurement Information System (PROMIS™), Sleep Disturbance (SF 8A)	**PTSD treatment resistant nightmares:** • 72% experienced cessation or significant decrease in nightmares • Suggested starting dose of 0.25mg of nabilone **Insomnia:** • Studied several CBD formulations against melatonin • All formulations led to significant improvements in sleep disturbance • CBD itself at low doses may be useful for improving sleep quality but the benefits do not exceed that of melatonin

Table 8. Recommendations for dosing and titrating in chronic pain[28]

Approach	Starting Cannabinoid Type	Starting Dose	Titration Regimen
Routine *Recommended for most patients	CBD Dominant	5mg CBD BID	• Increase CBD by 5mg per dose (10mg daily) every 2-3 days until effective • If patient does not reach treatment goals at dose of ≥ 40mg CBD per day, consider adding THC • Start at THC 2.5mg per day, increasing by 2.5mg every 2-7 days until treatment goals are met (max 40mg THC per day)
Conservative *For potentially more sensitive patients - clinically frail, comorbidities, mental health issues, polypharmacy	CBD Dominant	5mg CBD once daily or BID	• Increase CBD by 2.5mg-5mg per dose (5-10mg daily) every 2-3 days • If patient does not reach treatment goals at dose of ≥40mg CBD per day, consider adding THC • Start at THC 1mg per day, increasing by 1mg every 7 days until treatment goals are met (max 40mg THC per day)
Rapid *For urgent pain management – severe pain, palliative, significant prior use of cannabis	Balanced 1:1 (THC:CBD)	2.5-5mg of THC & CBD once daily or BID	• Increase THC & CBD by 2.5-5mg (once daily or BID) every 2-3 days, until treatment goals are met (max of 40mg THC per day)

REDUCING POLYPHARMACY & OPOID-SPARING EFFECTS

In recent years, the use of multiple chronic prescription medications or polypharmacy, has been highlighted as a major issue within medicine, and has been associated with an increased risk of negative health outcomes in patients.[33] This issue is especially pertinent for older adults, who are generally more sensitive to cumulative side effects and drug interactions, leading to an emphasis on deprescribing within the modern medical landscape.

Medical cannabis has significant potential to be a useful tool in the fight to deprescribe. As cannabis products may help improve multiple symptoms at once, including pain, sleep issues, anxiety and mood disturbances which are commonly comorbid, there is great potential to reduce the need for multiple prescription medications.[34] Although this evidence is promising, more research is needed to better understand these findings and how they fit into patient care.

- A recent observational study (N=535) from Australia looking at chronic pain patients, found that the total number of prescription medications patients took over 1 year decreased with the introduction of medical cannabis, including significant reductions in NSAIDs, benzodiazepines, and antidepressants.[34]
- In the 2023 Canadian Cannabis Survey 44% of medical cannabis users reported that it helped them reduce the use of other medications, most commonly opioids, non-opioid pain relievers, sedatives and anti-depressants.[7]
- Additionally, a 2022 systematic review & meta-analysis (92 studies) concluded that there is sufficient evidence from preclinical and observational data to demonstrate the potential for opioid-sparing effects of cannabinoids in the context of analgesia.[35]

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 concentrations of THC are more commonly associated with a higher risk of side effects.[23]

Table 9. Side effects associated with cannabis-based medicines containing high levels of THC[23]

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

OTHER WARNINGS AND PRECAUTIONS

Patients should not drive or operate machinery during and after the use of medical cannabis as it may cause unwanted side effects such as dizziness and or drowsiness.

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 practitioners have patients who are travelling with medical cannabis within Canada, ensure they are 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.

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] Cannabis dependency is divided into psychological and physical dependence and can occur particularly with chronic, heavy use, as outlined in the following chart.

Table 10. 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, headache, 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.[36] Tolerance for cannabis results from mostly pharmacodynamic and pharmacokinetic mechanisms and can be followed by withdrawal symptoms.[4] Tolerance for most cannabis effects may occur following a few doses and can quickly dissipate following discontinuation of the cannabis treatment.[4]

POTENTIAL DRUG-DRUG INTERACTIONS

When it comes to assessing for drug interactions, very different considerations need to be made when it comes to THC vs. CBD. 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] Additionally, co-administration with stimulants such as cocaine, MDMA, and amphetamines can lead to increased risk of tachycardia. Co-administration with drugs that are broken down by isoenzymes CYP2C9, CYP2C19, CYP34A can lead to interactions that would increase the bioavailability of THC and potentially increase 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]

In contrast, higher blood levels of CBD have been shown to inhibit CYP enzymes in the liver, including CYP2C9, CYP2C19, CYP2D6, CYP3A4, among others. This unique feature of CBD can potentially decrease how well certain prescription medications are metabolized, putting patients on medications (anticoagulants, anti-epileptics, etc.) with a narrow therapeutic index at risk.[37] For a comprehensive list of potential drug-drug interactions, please see the Canadian Health Care Professional guideline.

CLINICAL TOOLS

Drug-drug interactions are paramount and should be assessed before, during, and at the end of the treatment with medical cannabis. Some clinical tools can be consulted for extended support, such as the following:

Drug Interactions Checker: Medscape Drug Reference Database
(Link: https://reference.medscape.com/drug-interactionchecker)

Lexicomp: Evidence-Based Drug Referential Content
(Link: https://www.wolterskluwer.com/en/solutions/lexicomp)

The College of Family Physicians of Canada
(Link: https://www.cfpc.ca/CFPC/media/PDF/CFPC-Guidance-in-Cannabis-Within-Primary-Care.pdf)

Direct questions to hcp@mymedi.ca

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 dried flower, medical cannabis products are now 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 11. Properties of various medical cannabis delivery forms[4,11,23]

	Non-inhalable	Inhalable
Slow-acting Long-lasting	Oils, Capsules, Edibles, Topicals	N/A
Faster-acting Moderate lasting	Sublingual Sprays, Fast Release Capsules, Suppositories	Dried Flower, Vapes

AUTHORIZING MEDICAL CANNABIS USE

Below Are 5 Simple Steps Your Patients Can Follow to Access Medical Cannabis!

STEP 1

MEDICAL ASSESSMENT

Make an appointment with a healthcare professional (HCP) (e.g. family doctor or nurse practitioner) to be assessed for your suitability for medical cannabis.

If you do not have access to a family doctor, you may be assessed by an HCP at a specialty clinic either online or in-person found here:
(Link: https://mymedi.ca/get-started/)

STEP 2

AUTHORIZATION

You will be required to fill in the following medical document for your patient:

Medical Document Form
(Link: https://mymedi.ca/patients/)

STEP 3

SUBMISSION

Once completed you can send the medical document to us by secure fax or mail:

Secure Fax
1-844-500-4042

Mail
MyMedi.ca c/o Northern Green Canada
1-275 Orenda Road, Brampton
ON L6T 3T7

STEP 4

REGISTRATION

Typically it takes 1-2 business day to process the medical document after receiving from the HCP.

In the meantime, encourage your patient to complete their registration online or by submitting a paper or digital copy of the registration form to us so we can associate the medical document to their account.

Register Online
(Link: https://mymedi.ca/get-started/#register)
Downloadable Form
(Link: https://mymedi.ca/patients/)

STEP 5

ACCESS & ORDERING

Once medical documents are processed and the account is approved, the patient will then receive an email or call notifying them that they can place an order.

If the patient has any questions about the products, they can contact our expert Patient Support Team at 1-844-500-2040.

ⓘ ***DON'T FORGET***

Both healthcare practitioners and patients will have access to the trained staff and pharmacists at MyMedi.ca to provide clinical support when needed.

SUGGESTED RECOMMENDATIONS FOR USING CANNABINOIDS

HCPs may recommend cannabinoid-based products to treat a wide variety of conditions as listed in the section titled Current State of Evidence (see page 9). As mentioned, a comprehensive review of the evidence finds support for their use for conditions such as epilepsy, MS, anxiety, depression, insomnia, and some types of chronic pain.[15, 22] 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 and for more general use in symptom management.[38]

While anxiety, depression and sleep disorders may occur on their own as primary conditions without an underlying medical disorder, these conditions are extremely heterogeneous 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 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 12. Examples of product options for selected medical conditions

CBD Only	**High CBD Low THC**	**Moderate CBD Low THC**	**Balanced CBD and THC**	**THC Only**
CBD Only	Low Ratio THC:CBD (1:25)	Moderate Ratio THC:CBD (1:4)	High Ratio THC:CBD (1:2)	THC Only
• Severe Childhood Epilepsies (e.g. Dravet and Lennox Gastaut Syndromes)[25, 39] • Anxiety[40, 41] • Inflammation[42, 43]	• Severe Childhood Epilepsies (e.g. Dravet and Lennox Gastaut Syndromes)[25, 39] • Anxiety[40, 41] • Pain[43, 44] • PTSD[45] • Inflammation[42, 43]	• Pain[43, 44] • Multiple Sclerosis related spasticity[26, 46, 47] • Sleep[47, 48]	• Pain[43, 44] • Sleep[47, 48] • Chemotherapy induced Nausea & Vomiting[46]	• Pain[43, 44] • Sleep[47, 48] • Chemotherapy induced Nausea & Vomiting[46]

NOTE TO PRACTITIONERS

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]

MEDICAL CANNABIS AND RHO PHYTO

RHO Phyto's unique formulations have gone through 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. The RHO Phyto formulations are optimized for increased and faster absorption of cannabinoids relative to basic MCT (medium-chain triglyceride) oil formulations.

DID YOU KNOW?

Topical products may be designed to stay on top of the skin and target dermatological conditions or designed for transdermal absorption to target deeper musculoskeletal pain and other conditions. Practitioners should ensure that they, and their patients, are aware of the differences and select products accordingly. For more examples, refer to the explanations on our RHO Phyto topical products listed (see page 26 and 27).

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

Table 13. Quality standards and specifications used to guide RHO Phyto product development

	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 Process	Standardized meethods 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

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. All RHO Phyto formulations are designed to maintain the stability of the cannabinoids to ensure more consistent clinical effects over the course of treatment.

Table 14. RHO Phyto product range, cannabinoid ratios and the rate of relief

THC:CBD Ratios	CBD Only		1:25	1:20	1:10	1:4	1:2	1:1	THC Only
RHO Phyto Product	Micro Drop 100 CBD, Micro Drop 50 CBD	Rapid Act Spray 40 CBD, Rapid Act Capsules 50 CBD	Micro Drop 2:50 CBD	Rapid Act Spray 2:40 CBD	Nano Drop 5:50	Micro Drop 5:20 CBD	Rapid Act Spray 10:20 CBD	Rapid Act Balanced Capsules 5:5, Nano Drop Balanced 25:25	Micro Drop THC 20:0
Rate of Relief	Slow	Faster	Slow	Faster	Faster	Slow	Faster	Faster	Slow

RHO™

PHYTO

Deep Tissue	Ultra CBD	Micro Drop	Rapid Act	Rapid Act	Nano Drop	Daily Dose
GEL	CREAM	OIL	SPRAY	CAPSULES	OIL	GUMMIES

RHO PHYTO MICRO DROP OILS (30 mL)

RHO Phyto's Micro Drops are offered in a blood orange flavour and pomegranate 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 (Medium-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.

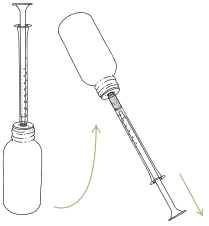
Micro Drop Oils are also available in tetrahydrocannabinol (THC)-Free formulas. They are designed to limit side effects commonly associated with THC and provide an alternative for users that would like to avoid products containing THC.

HOW TO USE

1

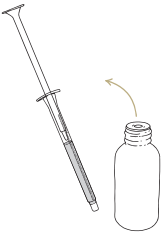
Press syringe into bottle adapter at the top of the bottle.

2



Once secure, turn the bottle upside down and gently pull on plunger of syringe to dispense desired amount of oil.

3



Once secure, turn the bottle upside down and gently pull on plunger of syringe to dispense desired amount of oil under your tonuge.

PRODUCT SPECIFICATIONS | MICRO DROP OILS

Product Specifications	Cannabinoid Ratio (w/w)	Size	Bottle Form	THC per mL	CBD per mL	Total THC	Total CBD
Micro Drop 100 CBD	CBD Only THC FREE	30 mL	Syringe	-	100 mg	-	3000 mg
Micro Drop 50 CBD	CBD Only THC FREE	30 mL	Syringe	-	50 mg	-	1500 mg
Micro Drop 2:50 CBD	1 THC : 25 CBD	30 mL	Syringe	2 mg	50 mg	60 mg	1500 mg
Micro Drop 5:20 CBD	1 THC : 4 CBD	30 mL	Syringe	5 mg	20 mg	150 mg	600 mg
Micro Drop THC 20	THC Only	30 mL	Syringe	20 mg	-	600 mg	-

SUGGESTED DOSING & TITRATION GUIDE

Day one: Start with 0.1 mL from the syringe style bottle orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 0.1 mL from the syringe style bottle 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 reassess 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.

ⓘ ***NOTE TO PRACTITIONERS***

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

RHO PHYTO RAPID ACT SPRAYS (15 mL)

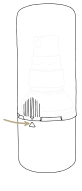
RHO Phyto's Rapid Act Sprays offered in lemon-mint flavour, are administered under the tongue to provide more direct absorption into the bloodstream by avoiding first pass metabolism by the gut and liver. RHO Phyto's Rapid Act Sprays are optimized for increased absorption and faster onset in comparison 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

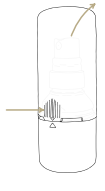
Shake well before using. For maximum absorption, hold spray under tongue for 30-90 seconds before swallowing. Please follow how to use instructions that correspond to your product bottle.

1



Align arrows on base with arrows on cap.

2



Squeeze at ridges on both sides and pull cap off bottle.

3

Remove secondary cap.

4

Spray under your tongue to dispense desired dose. Make sure to always put both caps back on bottle when finished.

PRODUCT SPECIFICATIONS | RAPID ACT SPRAYS

Each spray delivers 0.1 mL of sublingual spray for a total of 10 sprays per 1.0 mL.

Product Specifications	Cannabinoid Ratio (w/w)	Size	THC per mL	CBD per mL	CBG per mL	Total THC	Total CBD	Total CBG
Rapid Act Spray 40 CBD	CBD Only THC FREE	15 mL	-	40 mg	-	-	600 mg	-
Rapid Act Spray 10:20 CBD	1 THC : 2 CBD	15 mL	10 mg	20 mg	-	150 mg	300 mg	-
Rapid Act Spray 20:10 CBG	20 THC : 10 CBG	15 mL	20 mg	-	10 mg	300 mg	-	150 mg

SUGGESTED DOSING & TITRATION GUIDE

Day one: Start with 1 spray under the tongue (0.1 mL) orally in the early evening and assess the effect.

Days two to seven: Increase the daily dose by 1 spray (0.1 mL) 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 reassess 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.

ⓘ ***NOTE TO PRACTITIONERS***

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

DOSING GUIDE | RAPID ACT SPRAYS

	Amount (mg) of Cannabinoid per Spray (0.1 mL)		
Product Name	THC	CBD	CBG
Rapid Act Spray 40 CBD	-	4 mg	-
Rapid Act Spray 10:20	1 mg	2 mg	-
Rapid Act Spray 20:10 CBG	2 mg	-	1 mg

RHO PHYTO RAPID ACT CAPSULES (30 Capsules)

The Rapid Act Capsules from RHO Phyto are formulated using patented advanced self-emulsifying drug delivery system (SEDDS) technology, packaged in a convenient and discrete dosage form. The innovative nano-emulsion formulation was designed to increase the water solubility of large lipophilic cannabinoid molecules, to improve the absorption and speed of onset compared to basic MCT oil carriers. In addition, RHO Phyto's unique combination of ingredients maintains the stability of cannabinoids to ensure a reliable dose over time.

HOW TO USE

Patients may take the capsules with or without food, in the morning and/or the evening. For optimal efficacy, take at the same time each day.

PRODUCT SPECIFICATIONS | RAPID ACT CAPSULES

Product Specifications	THC : CBD Ratio	Size	THC mg/Capsule	CBD mg/Capsule	Total THC	Total CBD
Rapid Act Capsules 50 CBD	0:50 CBD THC FREE	30 Capsules	0 mg	50 mg	0 mg	1500 mg
Rapid Act Balanced Capsules 5:5	5:5 THC:CBD	30 Capsules	5 mg	5 mg	150 mg	150 mg

SUGGESTED DOSING

RHO PHYTO RAPID ACT CAPSULES 50 CBD

THC FREE

Day one: Start with 1 capsule once per day.

Days two to seven: Maintain the dose at 1 capsule once per day and monitor for safety and efficacy.

Days seven and onwards: Increase by 1 capsule **every 7 days** until an effective dose is reached that does not cause any unwanted side effects. If any side effects develop, lower the dose back to the previous one and reassess. A faster titration schedule may be necessary on a patient-by-patient basis, particularly in experienced users. The maximum recommended dose is 6 capsules per day (divided **twice to three times per day**).

RHO PHYTO RAPID ACT BALANCED CAPSULES 5:5

Day one: Start with 1 capsule once per day in the early evening.

Days two to seven: Maintain dose at 1 capsule once per day to assess the effect and tolerability.

Days seven and onwards: Increase dose by 1 capsule every 7 days until an effective dose is reached that does not cause any unwanted side effects. A faster titration schedule may be necessary on a patient-by-patient basis, particularly in experienced users. The maximum recommended dose is 6 capsules per day (divided **twice to three times per day**). If side effects develop, lower the dose to the previous one and reassess.

ⓘ ***NOTE TO PRACTITIONERS***

Please note that cannabis-naïve patients, older individuals and other susceptible clinical populations may experience significant THC-related side-effects even at low doses. Additionally, due to the enhanced absorption profile associated with this formulation, there may be stronger effects compared to typical MCT carrier oil formulations which should be considered in frail or naïve patients.

RHO PHYTO NANO DROPS (20 mL)

RHO Phytos' Nano Drops are offered in a unflavored water soluble drop that is formulated with tetrahydrocannabinol (THC) and cannabidiol (CBD). Nano Drops are prepared with high quality ingredients. It should be diluted before administration in a beverage of your choice such as water, tea, or juice etc. The product is administered with metered dosing using a metered dropper that allows accurate and easy titration.

HOW TO USE

Shake well before using. Press down firmly on cap and turn counterclockwise. Turn bottle upside down and lightly squeeze the body to dispense the desired number of drops.

PRODUCT SPECIFICATIONS | NANO DROPS

Each drop is 0.02 mL, for a total of 50 drops per 1.0 mL.

Product Specifications	Cannabinoid Ratio (w/w)	Size	Bottle Form	THC per mL	CBD per mL	Total THC	Total CBD	Per Drop
Nano Drop 5:50	1:10 THC:CBD	20 mL	Dropper	5 mg/g	50 mg/g	100 mg/g	1000 mg	0.1 mg THC 1 mg CBD
Nano Drop Balanced 25:25	1:1 THC:CBD	20 mL	Dropper	25 mg/g	25 mg/g	500 mg	500 mg	0.5 mg THC 0.5 mg CBD

RHO PHYTO DEEP TISSUE GELS (30 mL)

RHO Phyto's Deep Tissue Gels' patented technology 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 to ensure cannabinoid stability. 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.

PRODUCT SPECIFICATIONS | DEEP TISSUE GELS

Product Specifications	THC : CBD : CBG Ratio (w/w)	Size	THC mg/g	CBD mg/g	CBG mg/g	Total THC	Total CBD	Total CBG
Deep Tissue Gel	1:20 THC:CBD	50 mL	0.2 mg/g	5 mg/g	-	12.5 mg	250 mg	-
CBG Transdermal Gel	0.5:20:10 THC:CBD:CBG	25 mL	0.5 mg	20 mg	10 mg	12.5 mg	500 mg	250 mg

DOSING GUIDE | GELS

Each pump delivers 0.5 g of gel. Apply gel to affected area two to three times a day consistently to achieve desired effect.

	Volume Per Pump	THC	CBD	CBG
Deep Tissue Gel	0.5 mL	0.1 mg	2.5 mg	-
CBG Transdermal Gel	0.5 mL	0.25 mg	10 mg	5 mg

THC FREE

RHO PHYTO ULTRA CBD CREAM (30 mL)

This Ultra CBD Cream from RHO Phyto is formulated with 3% purified cannabidiol (CBD) and does not contain any THC. This advanced formulation was designed with ingredients to maintain cannabinoid stability and to increase absorption into skin layers. In addition, ingredients were selected with low irritant and allergen profiles with sensitive skin profiles in mind. Each Ultra CBD Cream is stored in pharmaceutical grade airless packaging, which provides protection from light and air to preserve the integrity of the product. Each 30 g bottle contains 900 mg of CBD. Each pump delivers 0.5 g of the cream (15 mg of CBD) to be applied topically.

HOW TO USE

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

PRODUCT SPECIFICATIONS | ULTRA CBD CREAM

Product Specifications	THC : CBD : CBG Ratio (w/w)	Size	THC mg/g	CBD mg/g	CBG mg/g	Total THC	Total CBD	Total CBG
Ultra CBD Cream	CBD Only	30 mL	-	30 mg	-	-	900 mg	-

DOSING GUIDE | ULTRA CBD CREAM

Each pump delivers 0.5 g of cream. Apply two to three times a day consistently to achieve desired effect.

	Per Pump	THC	CBD
Volume (mL)	0.5 mL	0	15 mg

THC FREE

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