

MEDICAL CANNABIS

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Disclaimer: This document is an interpretation of the Access to Cannabis for Medical Purposes Regulations (ACMPR) and the College of Physicians and Surgeons of Saskatchewan Bylaw 19.2. Please refer to latest legislation for up to date and complete information.

As of September 2016, over 98,000 Canadians are registered with Health Canada to obtain medical cannabis. This number has more than tripled since September 2015 when just over 30,000 clients were registered. It is estimated that this number will grow to 500,000 or more, within the next 10 years.

LEGISLATION AND REGULATIONS

- Schedule II, Controlled Drugs and Substances Act, cannabis is considered a “controlled substance”.
- Canadian regulations have changed over time:
 - **2001 - 2014: Marijuana Medical Access Regulations (MMAR):**
 - Patient use was authorized by Health Canada,
 - could only be prescribed for specific indications (e.g. chronic illness such as MS),
 - patients were legally able to grow once authorized,
 - and product safety/quality was not enforced (e.g. varying levels of THC).
 - **2013 to 2016: Marijuana for Medical Purposes Regulations (MMPR):**
 - Patient use must be authorized by a physician (or nurse practitioner in some jurisdictions),
 - medical marijuana could be prescribed for any indication,
 - patients must obtain marijuana or product from a licensed producer,
 - production became highly regulated, lab tested quality assurance.
 - Since June 2015, licensed producers can sell cannabis oil and fresh cannabis buds and leaves in addition to dried cannabis. Patients may legally possess cannabis in forms other than just dried leaves (e.g., they can make their own edibles).
 - **August 2016 to now: Access to Cannabis for Medical Purposes Regulations (ACMPR)**
 - New regulations in response to Federal Court ruling in Allard vs. Canada which declared the MMPR infringed upon the Canadian Charter of Rights, citing lack of reasonable access to medical cannabis for patients.
 - Patients can now obtain cannabis for medical purposes one of three ways:
 - A) Register with a licensed producer and receive their order in the mail (same method as under MMPR)
 - B) Register with Health Canada to produce their own cannabis
 - C) Register with Health Canada to designate someone else to produce cannabis for them
 - licensed producers may provide the seeds, growing supplies, and interim supply of cannabis for patients who choose to produce their own supply or designate someone else to.
 - Review <http://laws-lois.justice.gc.ca/eng/regulations/SOR-2016-230/index.html> for most current legislation.
- **“Compassion Clubs”, “dispensaries” or other unregulated store fronts selling marijuana are not licensed producers; they are unregulated establishments and clients may not be aware that purchases have not been legally attained.**
- **Minimum Prescribing Standards in Saskatchewan (College of Physicians and Surgeons of SK, Bylaw 19.2)**
 - Prescribing physician must be primary practitioner treating the condition cannabis is being used for.
 - Patient must sign a written treatment agreement with the prescribing physician.
 - Physicians must keep a separate record to provide to the College of Physicians and Surgeons.
 - Physicians may not store or dispense medical marijuana.
 - See Bylaw 19.2 for complete information:
<https://www.cps.sk.ca/imis/Documents/Legislation/Legislation/Regulatory%20Bylaws%20-%20August%202015.pdf>

PROCESS FOR OBTAINING MEDICAL CANNABIS

- Clients may:
 - purchase a supply from licensed producer
 - produce their own supply
 - designate a person to produce supply

- Clients must first consult with their physician to obtain a *medical document*: an authorization to purchase, often referred to as a prescription.
 - All physicians in Saskatchewan may write a medical document for medical cannabis. A sample medical document is available here: <http://www.hc-sc.gc.ca/dhp-mps/marihuana/info/med-eng.php>.
 - The medical document specifies the dosage and type of products the client may use.
 - The period of use stated in the medical document cannot exceed one year. Sample medical document: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/marihuana/info/med-eng.pdf
 - No list exists of physicians that are actively providing medical documents.
 - Nurse Practitioners may not prescribe medical cannabis in Saskatchewan.
- If purchasing, clients must register with a licensed producer of their choice. The most efficient method is for the physician to fax the medical document and completed registration application form from their office to the licensed producer.
 - The list of licensed producers and their contact information may be found here: <http://www.hc-sc.gc.ca/dhp-mps/marihuana/info/list-eng.php>
- If growing their own or having a designate grow their supply, clients must submit the original medical document and a registration application to Health Canada.
 - The Health Canada registration forms for growing are available at: <http://healthycanadians.gc.ca/alt/pdf/drugs-products-medicaments-produits/buying-using-achat-utilisation/cannabis-medical/access-acces/personal-production-personnelle/registration-form-formulaire-inscription-eng.pdf>
- Following registration with a licensed producer or Health Canada, the patient may order a cannabis product or the seeds and interim supply (if they choose to grow their own) from the licensed producer. The product will be shipped directly to the patient's home.
- Anecdotally, the time from submission of registration to time of delivery may be approximately 48 hours.

THERAPEUTICS

- The leaves and flowering tops of the cannabis plant contain at least 400 active non-cannabinoid compounds (e.g., terpenes, flavonoids) and more than 70 different cannabinoids.
 - Currently the two main therapeutic cannabinoids that have been identified are tetrahydrocannabinol (THC) and cannabidiol (CBD).
- The two most common species are Sativa (typically considered to be energizing) and Indica (considered to be more relaxing). Commercially available products may be hybrid combinations of species.

Human endocannabinoid system

- The endocannabinoid system has cannabinoid receptors throughout the body and is involved in a broad range of physiological processes. There are still other receptors not yet known.
 - *CB1 receptors*: predominantly expressed on the neurons in the brain and nervous system. Inhibits neurotransmitter release. Also found to a lesser extent in other areas, such as the adipose tissue, heart, lung, and bone.
 - *CB2 receptors*: predominantly expressed on the cells of the immune system.

Cannabis activity

- Tetrahydrocannabinol (THC):
 - Mixture of stimulant and depressant effects; this is the main cannabinoid that is psychoactive and create a "high".
 - elevated mood, relaxation, appetite, paranoia, depression, anxiety, hypertension, tachycardia
 - Partial agonist of CB1 and CB2 receptors.
 - Exists in the cannabis plant as mostly inactive THC-acid. Heating is required to decarboxylate the THC-acid into active THC.
- Cannabidiol (CBD):
 - Does not cause a psychoactive "high".
 - CBD does **not** bind significantly to CB1/CB2 receptors but affects activity of other enzymes and

- receptors.
- Potential anxiolytic, neuroprotective, anticonvulsant, analgesic, antiemetic and anti-inflammatory effects.
- Through an *entourage effect* may act synergistically with THC and may also lower the degree of psychoactivity caused by THC.

Pharmacokinetics:

- Highly lipophilic, wide distribution in tissues (large volume of distribution), long terminal half-life (4 days or longer), undergoes hepatic metabolism thus high clearance rates are associated with extensive first pass metabolism, excreted via biliary tract into feces along with urinary excretion of acid metabolites.
- *Smoking/vaporizing* cannabis has an onset within 3-10 minutes, higher blood levels, and a duration of action of 2-3 hours. Cannabis absorption and serum concentrations are influenced by the number, duration, and spacing of puffs, breath holding time, and inhalation volume.
- *Orally ingesting* cannabis has an onset of 60-90 minutes and typically lasts about 5-8 hours. Bioavailability and absorption are erratic, and dependent on gastric pH/administration in relation to foods.

Drug Interactions

- PK: THC induces CYP1A2; CBD inhibits CYP3A4 & 2D6.
- PD: potential for additive effect with CNS depressants and anticholinergics.

Dosing and Other Options

- Various surveys published in the peer-reviewed scientific and medical literature have suggested that the majority of people using smoked or orally ingested cannabis for therapeutic purposes reported using the equivalent of up to **three (3) grams of dried marijuana per day**, source: [Health Canada Information for Health Care Practitioners](#)
- 1 “joint” is usually 500-750 mg of dried cannabis. Medical cannabis costs approximately \$3- \$15/gram from a licensed producer depending on the ratios of THC:CBD.
- Given the erratic absorption and extensive first pass metabolism of orally ingested cannabis, doses need to be approximately 2.5x higher than smoked cannabis (oral dose of dried cannabis (mg) = 2.5x smoked dose (mg)). Note: this is not a direct conversion. If changing routes, suggest starting at low dose and titrating upwards to effect.
- Synthetic cannabinoids available in Canada include nabiximols (Sativex™) and nabilone (Cesamet™).
- **Dosing: Start Low, Go Slow** → No precise dose but inhaled is the most well studied route.
 - Average reported use is 1-3 grams per day, with Health Canada market data indicating an average of 2.6 grams per day.
 - The dose is highly individualized and relies on titration. First time users should consume their dose slowly by waiting at least 5 minutes between single puffs and waiting 2-3 hours between bites of oral products.
 - First time users may be at risk of overconsumption and undesirable effects.
 - Licensed producers have fixed ratio THC:CBD products for purchase.

USES:

- Conclusive or substantial evidence that cannabis or cannabinoids (includes both synthetic and plant-derived cannabinoids) are effective for:
 - Chronic pain in adults (cannabis)
 - Neuropathic pain: <34 mg THC/day associated with subjective improvement in refractory moderate intensity neuropathic pain in adults using concurrent analgesics.
 - Chemotherapy-induced nausea and vomiting (oral cannabinoids)
 - Patient-reported multiple sclerosis spasticity (oral cannabinoids)
 - Cannabis has only been studied in randomized control trials via the smoked/vaporized route, and only for chronic neuropathic pain.
- Moderate evidence that cannabinoids are effective for:
 - Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols)
- No large landmark trials.
- More than 150 reported uses, such as: anorexia/cachexia associated with HIV/AIDS or cancer, chronic pain syndromes (including cancer), anorexia nervosa, multiple sclerosis, spinal cord injury, bladder dysfunction associated with MS or spinal cord injury, amyotrophic lateral sclerosis, epilepsy, headache and migraine, arthritides (e.g., osteoarthritis, rheumatoid arthritis, spondylitis, gout, etc.) musculoskeletal disorders, fibromyalgia, dystonia, Huntington’s disease, Parkinson’s disease,

Tourette's syndrome, glaucoma, asthma, hypertension, anxiety and depression, sleep disorders, PTSD, Alzheimer's disease and dementia, inflammatory skin diseases (dermatitis, psoriasis, pruritis), GI system disorders (e.g., inflammatory bowel disease, hepatitis, pancreatitis, metabolic syndrome/obesity).

RISKS AND SIDE EFFECTS

- **Short Term Effects** (mostly linked to THC): dizziness, dry mouth, nausea, psychomotor deficits, increased risk of motor vehicle accidents, increased risk of falls in the elderly, associated with psychosis and higher THC doses associated with 5 fold risk of MI within 1 hour of smoking.
- **Long Term use:** Tolerance to some of cannabis' effects tends to develop after a few doses and also disappears rapidly following cessation. This includes effects on mood nausea, and the cardiovascular system but tolerance does not appear to develop for pain and spasticity. Tolerance is linked to the down regulation and desensitization of CB1 receptors.
 - Has effects on cardiovascular system (changes in blood pressure, heart rate, may increase risk of angina, exacerbate arrhythmias) and reproductive system.
 - Long-term users show deficits in prospective memory and executive function.
 - May be a trigger of psychotic events for individuals who are predisposed (e.g., schizophrenia, bipolar). Overall, effects on mental health unknown, use caution.
 - Risk of dependence and substance use disorder.
- Inhaled cannabis is not necessarily "safer than tobacco use": there are similar or higher amounts of carcinogens and polycyclic aromatic hydrocarbons. Cannabis users also tend to inhale more deeply and hold breath longer than tobacco smokers. Does not appear to cause COPD or increase risk of lung cancer but does cause symptoms of chronic bronchitis (cough, wheeze, phlegm) and may also decrease one's ability to fight infection (e.g., increased risk of pneumonia). Risk increases with higher doses and longer-term chronic use.
- **Special populations:**
 - **Adolescents:** Generally **CONTRAINDICATED** in less than 25 years of age because of structural brain development resulting in increased risk for schizophrenia and psychosis.
 - **Pregnancy:** No morphological abnormalities BUT potential loss of executive function at age 3 (inattentive, impulsivity, aggressive, difficulty problemsolving).

DOCUMENTATION

- At this time, "Dried marijuana is not an approved drug or medicine in Canada. The Government of Canada does not endorse the use of marijuana, but the courts have required reasonable access to a legal source of marijuana when authorized by a healthcare practitioner." (Health Canada)
- Cannabis is not a regulated prescription medication or natural product; it does not have a DIN or NPN, and therefore cannot be documented in PIP at this time. Pharmacists are encouraged to document its use on the patient's file when possible.
- Patients are provided with a "carrying card" with each purchase. This includes, amongst other details, the period of time in which the medical cannabis for that order is to be used for. A new carrying card, with a new date, is provided with each new supply.
 - Medical Cannabis is legal in Canada and patients should always carry their carrying card and registration documents; patients crossing international borders may face serious consequences importing medical cannabis.

RESOURCES

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