Cannabinoids for pain, or Opioids ...

**Trial evidence comparing cannabinoids and opioids is limited.**57 But they do have some similarities and differences to consider:

- **Efficacy:** For both drug classes, RCT evidence is of low quality and short duration, and tends to show only a modest reduction in pain. Longer trials tend to show less benefit. However, despite the relative lack of quality evidence, patients often have strong beliefs about the value of each drug class.
- **Adverse effects:** Nausea, sedation, and euphoria are adverse effects of both drug classes. Opioids can cause constipation;25 cannabinoids can cause psychiatric disturbances (e.g. anxiety, agitation, amotivation, psychosis).27 Adverse effects appear dose-related (↑ dose = ↑ AE). Both drug classes may be used by patients as an “escape”.
- **Addiction risk:** With prescription opioids, estimated to be 5.5%.28 With non-medical cannabis, estimated to be 9%.26 (The risk with medical cannabinoids is unstudied.)
- **Fatal overdose risk:** With prescription opioids, 0.23% with >100mg morphine per day (↑ risk with ↑ dose).29 With cannabis, fatal overdose risk appears to be negligible.1

**For both drug classes, the trial with an exit strategy is important.** Not all patients will respond to these medications.

---

**... Or Something Better?**

If patients are wanting an escape from pain – physical or emotional – there are better choices!

Non-pharmacological approaches to coping and living well with pain will be essential for success!
## Cannabinoids: Comparison Chart

### Medical Cannabis

<table>
<thead>
<tr>
<th>Name</th>
<th>Dosage Form</th>
<th>Indications &amp; Comments</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cannabinoids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Generic &amp; Trade Names</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cannabis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Indications &amp; Comments</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preferred over cannabis.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial: 0.25-0.5mg po HS</td>
<td></td>
<td>$22-18 g</td>
<td></td>
</tr>
<tr>
<td>Usual: 1mg po daily-BSI for CINV</td>
<td></td>
<td>$112.215 - $112 g</td>
<td></td>
</tr>
<tr>
<td>Usual max: 6mg/day</td>
<td></td>
<td>$310 g</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse Events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some notes on adverse effects:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- percentages below are often &quot;worst case scenarios&quot; from systematic reviews, yet due to trial-design issues could also be underestimates.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- adverse effects appear dose-related (↑dose = ↑AE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- it is difficult to compare AE rates between agents, due to few head-to-head trials.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- THC appears to be the main component responsible for causing a &quot;high&quot; (low-quality evidence).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- CBD possibly safer than THC, yet some of its psychotopic effects are underappreciated (e.g. vs placebo in predomminantly pediatric trials: aggression/agner 3-5% vs &lt;1%; irritability/ agitation 5-9% vs 2%; somnolence 25 vs 8%).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Prescribed Cannabinoids (pharmaceutical grade)

<table>
<thead>
<tr>
<th>Name</th>
<th>DOSING</th>
<th>Indications &amp; Comments</th>
<th>DOSING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cannabinoids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Critical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dronabinol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Indications &amp; Comments</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial: 2.5mg po HS</td>
<td>$7</td>
<td>e.g. 60mL bottle of oil containing 1200mg CBD =$130</td>
<td></td>
</tr>
<tr>
<td>Usual: 2.5mg po TID-QID for chemo nausea/vomiting (&quot;3mg/m&quot;)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5mg po BID ac lunch and supper for tinnitus AIDs 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max: 20mg/day</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

### Oral Cannabis Oils

<table>
<thead>
<tr>
<th>Name</th>
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</tr>
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<tr>
<td><strong>Cannabinoids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Indications &amp; Comments</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial: 2-3mg of CBD +/- THC po HS (e.g. 0.1mL of 20mg/mL CBD)</td>
<td>$7</td>
<td>e.g. 60mL bottle of oil containing 1200mg CBD =$130</td>
<td></td>
</tr>
<tr>
<td>Usual: Uncertain due to lack of randomized trials. Titrate slowly. (Consider: dronabinol &amp; nabimixins labeling suggest max doses of 25-30mg THC per day.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food increases absorption.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider 1st dose at 7 p.m. to leave time for assessing effect.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider weekend trial start (or when impairment less disaustrous).</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

### Dried Cannabis

<table>
<thead>
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<td></td>
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</tr>
<tr>
<td><strong>Indications &amp; Comments</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial: 1.2-puffs inhaled HS (1 puff of joint = 1-10mg THC. Variation is due to inhalation depth, puff size, THC potency, smoked vs vaped, joint size, etc.)</td>
<td>$12-24 for 1-2 puff HS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual: Uncertain due to poor quality evidence. Titrate slowly. Based on market data for 2017 in Canada, medical cannabis patients titrated themselves to an average dose of 750mg dried cannabis per day.</td>
<td>$180 for 750mg/day</td>
<td></td>
<td></td>
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<tr>
<td>3g/day</td>
<td></td>
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</table>
Who could be a candidate for cannabinoid therapy?

- **Cannabinoids are generally not considered first- to second-line therapy for any indication. Reserve use for patients who have failed other therapies.**
  
  - e.g. may consider if tried ≥3 drugs for neuropathic pain or ≥2 drugs for palliative pain or if refractory to standard therapies for CINV, spasticity in MS or SCI, or cachexia [or refractory pediatric seizure]

- **Watch for relative contraindications** such as pregnancy, breastfeeding, age <21-25, a history of psychoschizophrenia, or substance abuse history. For more details, see RxFiles Cannabis Q and A.

Prescribing/Authorizing Cannabinoids Safely

Cannabinoids are potential drugs of abuse; caution is needed when prescribing. In general, follow similar principles to prescribing opioids (see RxFiles Prescribing Opioids Safely). A summary of these principles is as follows:

- **Optimize suitable non-opioid therapies first** (drug and non-drug)
- **Check electronic health records** (e.g. PIP in SK) at baseline and with each visit
  
  Note: medical cannabis does not appear on PIP. Option to check order hx with Licensed Producer.

- **Document cannabis use on local EMR** (just like tobacco, alcohol, etc.).

- **Baseline urine drug screen, and randomly thereafter**

- **THC metabolite detected = THC-COOH. Note: urine drug screens in SK do not test for CBD.**

- **Assess risk of addiction, and monitor for cannabis use disorder**

- **Ensure the patient understands cannabinoids are prescribed as a trial**

  - Reasonable trial duration may be ~12 weeks.

- **Obtain Treatment Agreement and Informed Consent**

  - Search "agreement" at www.rxfiles.ca for a sample cannabis tx agreement.

  - Agreement includes safe storage – especially important if kids nearby!

- **Monitor for benefits & harms. Exit Strategy:** stop (often taper) if trial unsuccessful.

  - Possible taper to prevent withdrawal: ↓ by 25% q1week.

Monitoring for Cannabis Use Disorder (CUD)

| Prior to Tx: Screen for CUD | During Tx: Monitor for CUD | In primary care, watch for:
|----------------------------|----------------------------|-----------------------------|
| 1) Options for screening: | 1. rapid or un sanctioned dose ↑
| CUDIT-R specific to cannabis | Frequent changes needed | respiratory problems |
| CAGE-AID Questionnaire | Wants dried cannabis only | depression/amotivation |
| short & practical. | Wants high potency THC only | issues functioning/concentrating |
| 2) Diagnosing: | Misuse of other substances | (e.g. in studies, work, relationships) |
| use DSM-5 criteria. | Urine drug screen: aberrant | ____________________________ |
|                      | Concerns from friends/family | ____________________________ |
|                      | Poor functioning | ____________________________ |
|                      | (school/work/social) | ____________________________ |

Symptoms of Cannabis Withdrawal

(onset 1-2 days, peak 2-6 days)

- Anger, aggression, appetite change, weight loss, anxiety, irritability, restlessness, sleep disturbance, cannabis craving, physical discomfort.

Choosing Between Products

<table>
<thead>
<tr>
<th>Prescription Cannabinoids</th>
<th>via medical authorization</th>
<th>via retail sale</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g. nabihone, nabiximols</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quality Control</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regulated. Health Canada</td>
<td>In Saskatchewan, sellers from both medical &amp; retail streams use the same cannabis sources (a Health Canada licensed producer). Production standards exist, including testing for pesticides &amp; THC/CBD concentrations. However, similar to non-Rx herbal supplements, cannabis may have less vigorous production standards than Rx drugs.</td>
<td></td>
</tr>
<tr>
<td>pharmaceutical production standards in place (has Drug Identification Number).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dosing & Guidance

- **Standardized.**
- **Some indications and dosing are Health Canada approved.**
- **Will show up on the electronic medical record** (e.g. PIP in Saskatchewan).

- **Challenging. e.g. THC in 1 puff of cannabis joint can range from 1 to >10mg. No "studied usual dose".**

- **Prescriber may pick strain/ratio and max quantity allowed for patient. May limit duration, e.g. "one 60ml bottle of CBD oil, then see prescriber for further authorization."**

- **Overall, less control than prescription products** (e.g. "dosing interval" does not exist).

- **Note:** despite prescriber attempts to guide product and dosing, patients may supplement with cannabis products/buying from sellers from both medical & retail streams use the same cannabis sources (a Health Canada licensed producer). Production standards exist, including testing for pesticides & THC/CBD concentrations. However, similar to non-Rx herbal supplements, cannabis may have less vigorous production standards than Rx drugs.

Access

- **Dispensed by community pharmacy.**

- **Exclusively by mail/courier.**

- **At cannabis retail store; online ordering possible too.**

Paperwork Required for Medical Cannabis

1. Complete medical document form (link ❶).

2. Submit medical document to *Licensed Producer (link ❷)* who mails cannabis (dried, oil, buds, or leaves) to patient.

3. Or, patients may apply to grow their own product at home (e.g. 15 plants for 3g/day, see link ❸).

4. Medical document must be re-authorized at least once per year.

5. In SK, prescribers required to keep list of pts.

6. No set daily limit; max possession is lesser of 150g or 30 times daily amount.

- **Note:** despite prescriber attempts to guide product and dosing, patients may supplement with cannabis products/buying from sellers from both medical & retail streams use the same cannabis sources (a Health Canada licensed producer). Production standards exist, including testing for pesticides & THC/CBD concentrations. However, similar to non-Rx herbal supplements, cannabis may have less vigorous production standards than Rx drugs.

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The College’s bylaw which regulates physician authorization of medical marijuana is now in effect. The bylaw is numbered Bylaw 19.2 of the regulatory bylaws of the College and is available at the College’s website. Visit: http://www.cps.sk.ca/imis/CPSS/Programs_and_Services/Medical_Marijuana/Medical_Cannabis.aspx. A summary of the bylaw follows:

1. The bylaw begins with a statement that there has not been sufficient scientific or clinical assessment to provide evidence about the safety and efficacy of marijuana for medical purposes. The bylaw begins with an acknowledgement that federal government regulations have authorized the use of marijuana for medical purposes.

2. A physician cannot authorize the use of marijuana for a patient unless the physician is also the treating physician for the condition for which the patient is authorized to use marijuana. For example, if a patient is to be authorized to use medical marijuana to deal with symptoms of MS, the physician must also be the treating physician for the patient’s MS.

3. A physician must review the patient’s medical history, review relevant records pertaining to the condition for which the use of marijuana is authorized and conduct an appropriate physical examination before authorizing the patient’s use of marijuana.

4. The patient must sign a written treatment agreement which contains the following:
   A) A statement from the patient that the patient will not seek a prescription for marijuana from any other physician during the period for which the marijuana is prescribed;
   B) A statement by the patient that the patient will utilize the marijuana as prescribed, and will not use the marijuana in larger amounts or more frequently than is prescribed;
   C) A statement by the patient that the patient will not give or sell the prescribed marijuana to anyone else, including family members;
   D) A statement by the patient that the patient will store the marijuana in a safe place

Sample treatment agreement: http://www.cps.sk.ca/iMIS/Documents/Programs%20and%20Services/Patient%20Agreement%20Template%20-%20Medical%20Cannabis.pdf
Or visit www.RxFiles.ca and search "agreement".

5. The physician’s record for the patient must include the requirements for all medical records and, in addition, contain the following:
   A) The treatment agreement signed by the patient;
   B) The diagnosis for which the patient was authorized to purchase marijuana;
   C) A statement of what other treatments have been attempted for the condition for which the use of marijuana was prescribed and the effect of such treatments;
   D) A statement of what, if anything, the patient has been advised about the risks of the use of marijuana;
   E) A statement that in the physician’s medical opinion the patient is likely to receive therapeutic or palliative benefit from the use of marijuana to treat the patient’s condition.

6. The physician must retain a single record, separate from other patient records, which can be inspected by the College, and which contains:
   A) The patient’s name, health services number and date of birth;
   B) The quantity and duration for which marijuana was prescribed;
   C) The medical condition for which marijuana was prescribed;
   D) The name of the licensed producer from which the marijuana will be obtained, if known to the physician.

7. Physicians who prescribe marijuana will be required to provide the College with the information referenced in paragraph 6:
   A) Every twelve months if the physician has prescribed marijuana to fewer than 20 patients in the preceding 12 months;
   B) Every six months if the physician has prescribed marijuana to 20 or more patients in the preceding 12 months.

8. The bylaw prohibits physicians from diagnosing or treating patients at the premises of a licensed producer;

9. The bylaw prohibits physicians who prescribe marijuana from having an economic or management interest in a licensed producer;

10. The bylaw prohibits physicians from storing or dispensing marijuana from any location where the physician practices medicine.
Submitting Adverse Effect information to Health Canada:

Tips on filling out Part D (for cannabis products i.e. dried cannabis or cannabis oils)

- DIN or NPN is **not** required
- Include: brand name, strain name, lot #, licensed holder name, intended use (medical or non-medical)
- If the product was not purchased from a legal retailer it can still be reported but it would be useful to indicate if it was purchased from a non legal source so it can be processed properly in our database.
References: Cannabinoid Chart – www.RxFiles.ca


35. Aldington S, Williams M, Nowitz M, Weatherall M, Pritchard A, McNaughton A, Robinson G, Beasley R. THE EFFECTS OF CANNABIS ON PULMONARY STRUCTURE, FUNCTION AND SYMPTOMS. Thorax. 2007 Jul 31; [Epub ahead of print] Smoking cannabis was associated with a dose-related impairment of large airways function resulting in airflow obstruction and hyperinflation. In contrast, cannabis smoking was seldom associated with macroscopic emphysema. The 1:2.5 to 5 dose equivalence between cannabis joints and tobacco cigarettes for adverse effects on lung function is of major public health significance.


Additional references for Cannabinoids:


of efficacy, THC preparations should be considered still experimental, with some positive effects on withdrawal symptoms and craving. The evidence base for the anticonvulsant gabapentin, oxytocin, and N-acetylcycteine is weak, but these medications are also worth further investigation.


Starzer MSK, Nordenfont N, et al. Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis. Am Psychiatry. 2017 Nov 28;appiajp201717020223. (Cannabis etc.)


Tan WC, Sin DD. What are the long-term effects of smoked marijuana on lung health? CMAJ. 2018 Oct 22;190(42):E1243-E1244.


