Cannabis Patient Booklet may be a useful tool (available online ©www.RxFiles.ca)

Cannabis edibles aren’t legal for purchase [yet].

... 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!

Cannabis 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;21 cannabinoids can cause psychiatric disturbances (e.g. anxiety, agitation, amotivation, psychosis).27 Adverse effects appear dose-related (↑ dose = ↑ AE).27 Both drug classes may be used by patients as an “escape”.
- **Addiction risk:** With prescription opioids, estimated to be 5.5%.26 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).25 With cannabis, fatal overdose risk appears to be negligible.1

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

Miscellaneous info: Synthetic illicit cannabinoids: e.g. K2, Spice – highly potent CB1/CB2 receptor agonists; case reports of severe acute toxicity.34 Phytocannabinoids: a cannabinoid derived from cannabis (e.g. THC, CBD, & others). THC: a partial CB1 & CB2 agonist; CBD: uncertain mechanism of action. Entourage effect: an unproven hypothesis that efficacy of cannabinoids is increased (or adverse effects decreased) when they are used in combination and/or in particular ratios and/or with flavonoids, terpenoids. Topical cannabis: e.g. creams: an unproven dosage form, promoted as local analgesia without systemic effect, but currently without trials to support. Concentrated Cannabis e.g. hash, shatter, badder, wax: contains THC as high as 90%. Dabbing: vaping small amounts of concentrated marijuana. Travelling with cannabis outside of Canada: not recommended. Non-medical cannabis: aka “recreational”. Is cannabis opioid-sparing? Evidence is still unclear.58-66
### Cannabinoids: Comparison Chart

#### Medical Cannabis

<table>
<thead>
<tr>
<th>Generic/TRADE</th>
<th>Indications &amp; Comments</th>
<th>DOSING</th>
<th>$/30d</th>
<th>Adverse Events AE</th>
<th>Contraindications CI</th>
<th>Drug Interactions M</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nabiximols SATIVEX</strong></td>
<td>Extracted THC/CBD</td>
<td>2.7mg THC &amp; 2.5mg CBD per spray (peppermint flavour; poor taste) (contains alcohol)</td>
<td>3 vial pack = $700 (56.20/spray) (30 sprays/vial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cannabinoids EPIDIOLEX</strong></td>
<td>Extracted CBD</td>
<td>100mg/mL solution</td>
<td>Not available in Canada</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Dronabinol MARINOL</strong></td>
<td>Synthetic THC</td>
<td>USA only: 2.5, 5mg, 10 cap (in sesame oil)</td>
<td>5mg/mL solution</td>
<td>D/C from Canadian market</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral Cannabins</strong></td>
<td>THC/CBD in various ratios,</td>
<td>25mg THC / 0mg CBD per mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dried Cannabis</strong></td>
<td>THC/CBD in various ratios,</td>
<td>25mg THC / 0mg CBD per mL</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

#### Prescription Cannabis (pharmaceutical-grade)

<table>
<thead>
<tr>
<th>Generic/TRADE</th>
<th>Indications &amp; Comments</th>
<th>DOSING</th>
<th>$/30d</th>
<th>Adverse Events AE</th>
<th>Contraindications CI</th>
<th>Drug Interactions M</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nabimethyles CESAMET</strong></td>
<td>Preferred over cannabis, off-label: AID-related anoxia</td>
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<tr>
<td><strong>Nabimethyles SATIVEX</strong></td>
<td>Advanced cancer pain (adjunctive)</td>
<td></td>
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</tr>
<tr>
<td><strong>Cannabinoids EPIDIOLEX</strong></td>
<td>Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients ≥ 2 years of age</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dronabinol MARINOL</strong></td>
<td>Seizures (Lennox-Gastaut or Dravet): 2.5-10mg/kg/dose per BID usually given before a meal</td>
<td></td>
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<tr>
<td></td>
<td>Food increases absorption.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Oral Cannabins</strong></td>
<td>Severe nausea/vomiting from cancer chemotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dried Cannabis</strong></td>
<td>Severe nausea/vomiting from cancer chemotherapy</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

### Notes
- **AE:** Some notes on adverse effects:
  - Percentages below are often "worst case scenarios" from systematic reviews, yet due to trial-design issues could also be underestimates.
  - Adverse effects appear dose-related ( ↑ dose → ↑ AE)
  - It is difficult to compare AE rates between agents, due to few head-to-head trials.
  - THC appears to be the main component responsible for causing a "high" (low-quality evidence).
  - CBD possibly safer than THC, but some of its psychotropic effects are underappreciated (e.g. vs placebo in predominately pediatric trials: aggression/agner 3-5% vs 1%; irritability/agitation 5-9% vs 2%; somnolence 25% vs 8%).
- **drowsiness or sedation up to 50% across cannabinoids.**
- **dizziness up to 32% across cannabinoids.**
- **psychiatric disturbances up to 17% across cannabinoids,** and up to 27% with inhaled cannabinoid. **THC** including depression, anxiety, panic, paranoia, hallucination. **Euphoria** up to 15%, and feeling "high" up to 35% across cannabinoids.
- **acute psychosis or dissociation up to 5% across cannabinoids.**
- **speech disorders up to 32%, and ataxia up to 30% across cannabinoids.**
- **impaired memory up to 11% across cannabinoids.**
- **irritability or agitation up to 9%, and anger or aggression** up to 5% with CBD.
- **appetite changes:** decreased appetite in up to 22% of patients on CBD, but conversely increased appetite in up to 38% of patients on dronabinol.
- **GI issues:** dry mouth; diarrhea up to 20%, vomiting up to 15% with CBD. **Conversely:** nausea in up to 20% of pts with dronabinol. **SATIVEX:** mouth irritation, pneumonia up to 8% with oral CBD.
- **LFTs up to 16% of pts on CBD:** related to concomitant valproate/clobazam.
- **driving impairment:** risk of fatal car crash approximately doubles with THC. **Cardiovascular issues** (e.g. ↑ HR, ↑ postural hypotension, ↑↑ MI 1 hour after smoking, ↑↑↑ MI 1 hour after smoking); also depression, anxiety, panic, paranoia, hallucination.
- **speech disorders:** related to impairment studies have focused on THC component; history of seizures, psychiatric disorders (e.g. bipolar, anxiety), cardiovascular disease, or respiratory disease.
- **A note on drug interactions:** Interactions are not fully understood; many are theoretical. Cannabis has many compounds besides THC & CBD; these may have unknown drug interactions. Watch closely for pharmacodynamic (additive) interactions.

### Other Information
- **Cannabinoids:** associating CNS effects (e.g. sedation, confusion, impairment) with alcohol, anticholinergics, anti-epileptics, benzos, opioids, etc.
- **THC-containing products 2CD & 3AD substrates:** levels by CBZ, SWJ, phenytoin, etc.
- **CBD-containing products 2CD & 3AD substrates:** levels by CBZ, SWJ, phenytoin, etc.
- **Smoked cannabis:** smoking may result in 1A2 induction; e.g. ↓ levels of antipsychotics, caffeine, TCAs, theophylline, warfarin
- **Medical cannabis:** while a THC-mimic, does not have THC drug interactions.

### References
- Crawley BSP, M Lebras Pharm D, L Regier BSP, B Jensen BSP. **© www.RxFiles.ca Oct 2018**
### Who could be a candidate for cannabinoid therapy?

- Cannabinoids are generally not considered first- or 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 psychosis/schizophrenia, 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-cannabinoid 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. Urine: urine drug screens in SK do not test for CBD.
- **Assess risk of addiction, and monitor for cannabis use disorder**
- **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 [87]
- **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)

- **9% of adults who use cannabis non-medically develop addiction (& up to 17% if started in adolescence).**

#### Prior to Tx: Screen for CUD

1. **Options for screening:**
   - **CUDIT-R** specific to cannabis. [45]
   - **CAGE Questionnaire** short & practical. [46]
2. **Diagnosing:**
   - use DSM-5 criteria. [53]

#### During Tx: Monitor for CUD

- **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 e.g. nabilone, nabiximols</th>
<th>Cannabis</th>
</tr>
</thead>
<tbody>
<tr>
<td>via medical authorization</td>
<td>via retail sale</td>
</tr>
<tr>
<td><strong>Quality Control</strong></td>
<td><strong>Patient selects the product, dose, dosing interval, and route of administration.</strong></td>
</tr>
<tr>
<td>Regulated. Health Canada pharmaceutical production standards in place (has Drug Identification Number).</td>
<td><strong>Difficult to provide monitoring, boundaries, or education.</strong></td>
</tr>
<tr>
<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>
</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".
- **Physician may pick strain/ratio and max quantity allowed for patient. May limit duration, e.g. "one 60mL bottle of CBD oil, then see physician for further authorization."**
- **Overall, less control than prescription products (e.g. "dosing interval" does not exist).**

### 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).

#### Paperwork Required for Medical Cannabis

- **Quality Control**
- **Dosing & Guidance**
- **Access**
- **Paperwork**
- **Coverage**

### Notes

- **Note:** currently Canada has a "two-stream" cannabis system: medically authorized cannabis, and cannabis through retail sale.

- **EDS in SK:** priority approval NIHB, not covered SK
- **EDS in Quebec:** not covered NIHB
The College’s bylaw which regulates physician authorization of medical marihuana 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/CPSS/Programs_and_Services/Medical_Marijuana/Medical_Cannabis.aspx](http://www.cps.sk.ca/imis/CPSS/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 marihuana for medical purposes. The bylaw begins with an acknowledgement that federal government regulations have authorized the use of marihuana for medical purposes.

2. A physician cannot authorize the use of marihuana for a patient unless the physician is also the treating physician for the condition for which the patient is authorized to use marihuana. For example, if a patient is to be authorized to use medical marihuana 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 marihuana is authorized and conduct an appropriate physical examination before authorizing the patient’s use of marihuana.

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 marihuana from any other physician during the period for which the marihuana is prescribed;
   B) A statement by the patient that the patient will utilize the marihuana as prescribed, and will not use the marihuana 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 marihuana to anyone else, including family members;
   D) A statement by the patient that the patient will store the marihuana in a safe place

Sample treatment agreement: [http://www.cps.sk.ca/iMIS/Documents/Programs%20and%20Services/Patient%20Agreement%20Template%20-%20Medical%20Cannabis.pdf](http://www.cps.sk.ca/iMIS/Documents/Programs%20and%20Services/Patient%20Agreement%20Template%20-%20Medical%20Cannabis.pdf)

Or visit [www.RxFiles.ca](http://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 marihuana;
   C) A statement of what other treatments have been attempted for the condition for which the use of marihuana 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 marihuana;
   E) A statement that in the physician’s medical opinion the patient is likely to receive therapeutic or palliative benefit from the use of marihuana 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 marihuana was prescribed;
   C) The medical condition for which marihuana was prescribed;
   D) The name of the licensed producer from which the marihuana will be obtained, if known to the physician.

7. Physicians who prescribe marihuana will be required to provide the College with the information referenced in paragraph 6:

   A) Every twelve months if the physician has prescribed marihuana to fewer than 20 patients in the preceding 12 months;
   B) Every six months if the physician has prescribed marihuana 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 marihuana from having an economic or management interest in a licensed producer;

10. The bylaw prohibits physicians from storing or dispensing marihuana from any location where the physician practices medicine.
References: Cannabinoid Chart – www.RxFiles.ca


Additional references for Cannabinoids:


