Cannabis: Overview

Clinical Pearls
- Routinely ask about cannabis use in primary care (just like tobacco and alcohol), & monitor for cannabis use disorder.
- After failure of ≥3 other drugs, a trial of prescription cannabinoids (rather than cannabis) may be reasonable for treating neuropathic pain.2
- Approach cannabinoids with similar caution as opioids – see box below.
- Start cannabinoids at a low dose, and gradually titrate. A few clinical trials suggest some efficacy even at very low doses,12,22 Adverse effects are common; monitor; stop or taper if not tolerated.
- Inhaled cannabis is not a preferred route of administration due to difficulty dosing, risk of respiratory damage, and multi-component composition.
- Medical cannabis is not recorded on PIP in Saskatchewan (Rx-cannabinoids are).
- The potential harms of cannabinoids are often underappreciated by patients. Informed consent and patient education are advisable. The RxFiles Cannabis Patient Booklet may be a useful tool (available online 🌐).

 Definitions and Background Information

Cannabinoid receptors: CB1 receptors (primarily in the central and peripheral nervous systems) and CB2 receptors (primarily in the immune system) are part of an endocannabinoid system in humans.1

Cannabinoids: compounds that activate cannabinoid receptors. Endogenous cannabinoids in humans include AEA & 2-AG. Two studied, although still poorly understood, cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).

Cannabis: aka marijuana. Contains 400+ compounds, including 140+ cannabinoids. Often marketed based on THC & CBD concentrations, although it is uncertain if these are the most important compounds in cannabis.

Prevalence (2019): 18% of Canadian adults used cannabis in last 3mos, 6% used daily, & 2% were registered for medical use.16,30

Challenges with the evidence: limited & small RCTs, of short duration, studying differing routes, forms & types of cannabinoids results in low confidence in assessing benefits & harms. Trials with longer duration tend to show less benefit,11 implying that if an effect exists, it may wear off over time. Further, few cannabis trials are adequately blinded due to the psychotropic effects of cannabinoids (~90% of patients can guess their allocation),13 which is thought to bias results toward benefit.17

Current (2020) legal status in Canada: Rx cannabinoids are Schedule II (controlled substances). Dried cannabis & oils are legal from licensed producers with Rx authorization (“medical cannabis”), or from a cannabis retail store. Some edibles/topicals are legal (2019).
Cannabinoids: Comparison Chart

<table>
<thead>
<tr>
<th>Medical Cannabis</th>
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<tbody>
<tr>
<td>Source: personal observations, published reports, governmental reports, websites on cannabis, and review articles.</td>
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### Cannabinoids

#### Prescription Cannabis

**Nabilone**
- **Generic**: CESAMET, g
- **Synthetic THC analogue**
- **Thc**: 0.5 mg cap
- **2 mg/mL suspension**: (contains alcohol)
- **Adverse Events**: HR, BP, CNS adverse effects, psych symptoms, tx agreement, CUD, LFTs

**Nabiximols**
- **Generic**: SATIVEX, x
- **Extraction**: THC/CBD
- **2.7mg THC & 2.5mg CBD per spray**: (peppermint flavor; poor taste)
- **Usual**: 2.5mg THC / 0mg CBD per spray
- **Usual max**: 12 sprays per day

**Cannabidiol**
- **Generic**: EPIDIOLEX
- **Extraction**: CBD
- **100mg/mL solution**: (contains alcohol, sesame oil; strawberry flavor)
- **Usual**: 2.5 mg/kg/day

**Dronabinol**
- **Generic**: MARINOL
- **Synthetic THC**
- **Usual**: 750mg/day

#### Oral Cannabis Oils

- **Generic**: THC/CBD in various ratios
- **Usual**: 25mg THC / 0mg CBD per mL
- **Usual max**: 150mg THC / 5mg CBD per mL

#### Dried Cannabis

- **Generic**: THC/CBD in various ratios
- **Usual**: 25mg THC / 0mg CBD per mL

### Indications & Comments

<table>
<thead>
<tr>
<th>Cannabinoids (pharmaceutical grade)</th>
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| **Cannabis**

| Usage: | Preferred over cannabis, CIP^18
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<tr>
<th align="center">:--:</th>
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<tbody>
<tr>
<td align="center"><strong>Severe nausea/vomiting from cancer chemotherapy</strong></td>
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<td align="center"><strong>Side effects</strong></td>
<td align="center"><strong>Side effects</strong></td>
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<tr>
<td align="center"><strong>Neuropathic pain</strong></td>
<td align="center"><strong>Neuropathic pain</strong></td>
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<tr>
<td align="center"><strong>Not detected in SK urine drug screen</strong></td>
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| Usage: | Preferred over cannabis, CIP^18
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<tr>
<td align="center"><strong>Advanced cancer pain (adjunctive)</strong></td>
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<td align="center"><strong>Multiple sclerosis neuropathic pain or spasticity (adjunctive)</strong></td>
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<tr>
<td align="center"><strong>Spasticity may require lower doses than pain</strong></td>
<td align="center"><strong>Spasticity may require lower doses than pain</strong></td>
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<tr>
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<tr>
<td align="center"><strong>Neuropathic pain</strong></td>
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| Usage: | Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients ≥ 2 years of age
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<tr>
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<tr>
<td align="center"><strong>Lennox-Gastaut or Dravet</strong></td>
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<tr>
<td align="center"><strong>2-year-old</strong></td>
<td align="center"><strong>2-year-old</strong></td>
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<td align="center"><strong>Not detected in SK urine drug screen</strong></td>
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| Usage: | Initial: 2.5-10mg po/p.o. / 2.5mg po H/S
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| Usage: | Initial: 2.5-30mg po/daily
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| Usage: | Initial: 0.25-0.5mg po H/S
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<tbody>
<tr>
<td align="center"><strong>Seizures</strong></td>
<td align="center"><strong>Seizures</strong></td>
</tr>
<tr>
<td align="center"><strong>Adjunctive</strong></td>
<td align="center"><strong>Adjunctive</strong></td>
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<tr>
<td align="center"><strong>Not detected in SK urine drug screen</strong></td>
<td align="center"><strong>Not detected in SK urine drug screen</strong></td>
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### Usual Dosing

<table>
<thead>
<tr>
<th>Dosing</th>
<th>$/30d</th>
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<tbody>
<tr>
<td><strong>250mg CBD oil</strong></td>
<td>$22-18 g</td>
</tr>
<tr>
<td><strong>1-2mg po daily</strong></td>
<td>$112-215 g</td>
</tr>
<tr>
<td><strong>1mg BID for neuropathic pain</strong></td>
<td>$112 g</td>
</tr>
<tr>
<td><strong>6mg/day</strong></td>
<td>$310 g</td>
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</tbody>
</table>

### Adverse Events

- Overall: The most common adverse events are increased appetite, dry mouth, drowsiness, and dizziness. Other common events include nausea, sedation, fatigue, dizziness, and euphoria.

### Contraindications

- **Use with caution** in patients with certain medical conditions, such as cardiovascular disease, respiratory disease, glaucoma, or those who are breastfeeding.

### Drug Interactions

- **Avoid** concurrent use with MAO inhibitors, methylxanthines, or strong CYP3A4 inhibitors.

### Side Effects

- **Common**: Drowsiness, dry mouth, dizziness, fatigue, sedation, and euphoria.

### Drug-Drug Interactions

- **Avoid** concurrent use with MAO inhibitors, methylxanthines, or strong CYP3A4 inhibitors.

### Pregnancy

- **Category**: C
d

### Breastfeeding

- **Caution**: Contraindicated

### Caution

- **Avoid** concurrent use with MAO inhibitors, methylxanthines, or strong CYP3A4 inhibitors.

### Mutagenesis

- **Category**: C

### Carcinogenesis

- **Category**: C

### Developmental and Fetal Toxicity

- **Category**: C

### Lactation

- **Category**: C

### Teratogenicity

- **Category**: C

### Mutagenesis

- **Category**: C

### Carcinogenesis

- **Category**: C

### Developmental and Fetal Toxicity

- **Category**: C

### Teratogenicity

- **Category**: C

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**Note**: The information provided is for educational purposes only and should not be used as a substitute for professional medical advice. Always consult a healthcare professional for diagnosis and treatment of any health condition.
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. In general, follow similar principles to prescribing opioids (see page 130). A summary of these principles is as follows:

- Optimize suitable non-cannabinoids therapy first (drug and non-drug)  
- Check Prescription Drug Monitoring Programs (e.g. PIP in SK) at baseline & at each visit  
  These programs do not record medical cannabis. 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 cannabinoid 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
  1) Options for screening:
     - CUDIT-R: specific to cannabis.  
     - CAGE-AID Questionnaire short & practical.
  2) Diagnosing: use DSM-5 criteria.

- During Tx: Monitor for CUD
  - rapid or unsanctioned dose ↑  
  - frequent changes needed  
  - wants dried cannabis only  
  - wants high potency THC only  
  - misuse of other substances  
  - urine drug screen: aberrant  
  - concerns from friends/family  
  - poor functioning (school/work/social)  
  - missed follow-up; reports of lost or stolen cannabis

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>Cannabis</th>
</tr>
</thead>
<tbody>
<tr>
<td>via medical authorization</td>
<td>via retail sale</td>
</tr>
<tr>
<td>Quality Control</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 rigorous production standards than Rx drugs.</td>
</tr>
<tr>
<td>Dosing &amp; Guidance</td>
<td>Challenging. e.g. THC in 1 puff of cannabis joint can range from 1 to &gt;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. &quot;dosing interval&quot; does not exist).</td>
</tr>
<tr>
<td>Access</td>
<td>Patient selects the product, dose, dosing interval, and route of administration.</td>
</tr>
<tr>
<td>Paperwork Required for Medical Cannabis</td>
<td>Difficult to provide monitoring, boundaries, or education.</td>
</tr>
<tr>
<td>Coverage</td>
<td>Note: despite prescriber attempts to guide product and dosing, patients may supplement with retail cannabis against medical advice.</td>
</tr>
</tbody>
</table>

Paperwork Required for Medical Cannabis

1. Complete medical document form (link ❶): In SK, complete treatment agreement form (link izzasite), or visit RxFiles.ca and search “agreement”.
2. Submit medical document to Licensed Producer (link ❷) who mails cannabis (dried, oil, buds, or leaves) to patient.
3. Or, patients may 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.


Cannabis pricing estimates (in Canada) from 2-Arachidonoylglycerol (2-AG) to 2-Arachidonylethanolamine (AEA): $6-15/gd (dried, oil, buds, or leaves). Cost of cannabis products vary. Refer to RxFiles Cannabis Q and A for more.

Cannabinoids: Prescribing Considerations

A Crawley BSP, M LeBras Pharm D, L Regier BSP © www.RxFiles.ca Apr 2020
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.cps.sk.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.
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.


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.


