Cannabinoids: Overview [1-8]

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Clinical Pearls

- Routinely ask about cannabis use in primary care (just like tobacco/alcohol), & monitor for cannabis use disorder (up to 1 in 5 may develop with ongoing use).[76,77]
- After failure of ≥3 other medications, 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.[21,22] Adverse effects are common; monitor & document; stop or taper if not tolerated.
- Inhaled cannabis (esp. smoked) is not a preferred route due to difficulty dosing, risk of respiratory damage, and multi-component composition.
- 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 recommended. See the RxFiles Cannabis Patient Booklet (available online: colour, or B/W 💻, or print copy).

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 the endocannabinoid system in humans.[1]

Cannabinoids: compounds that activate cannabinoid receptors. Endogenous cannabinoids in humans include AEA & 2-AG. Two studied, although still not well understood, cannabinoids are delta-9-tetrahydrocannabinol (**THC**) and cannabidiol (**CBD**).

Cannabis (aka *marijuana)*: Contains 400+ compounds, including 140+ cannabinoids. Marketed based on concentration of THC & CBD, though it is uncertain if these are the only important compounds in cannabis (e.g. Potential "entourage effect": see Misc. info below).

Prevalence (2021): 25% of Canadians ≥16 yrs used cannabis in last 12mos, 19% used daily, & 3% have HCP auth for medical use.[85]

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 cannabinoid trials are *adequately blinded* due to the psychotropic effects of cannabinoids (~90% of patients can guess their allocation),[11] which is thought to bias results toward benefit.[17]

Legal status in Canada: Rx cannabinoids are Schedule II in Controlled Drug & Substances Act. Dried cannabis & oils are legal from licensed producers with HCP authorization ("cannabis for medical purposes"), or from a cannabis retail store. Some edibles (<10mg THC)/topicals are legal.

Do Cannabinoids Work (For Medical Purposes)?

Cannabinoids may (limited, low quality evidence for benefit, compared to placebo):

- ↓ chronic neuropathic pain **NNT=11** for ≥30% reduction over ~4 wks.[2,15]
  {Balance of evidence for ?↓pain, but some ↑harms → shared decision making} [78,79]
- ↓ chemotherapy-induced nausea & vomiting
  NNT=3 for control of nausea/vomiting over ~1 day.[2]
- ↓ spasticity of multiple sclerosis or spinal cord injury
  NNT=10 for ≥30% ↓ spasticity over ~6 wks.[68]
- ↓ seizures in Lennox-Gastaut & Dravet syndrome with CBD
  NNT=4-7 for ≥50% reduction in seizure frequency over ~14 wks.[2]
- ↓ cachexia in HIV/AIDS, cancer, palliative care: weak evidence.

Clinical practice guideline (for chronic pain):[BMJ '21] If standard care not sufficient, trial non-inhaled medical cannabinoids. Potential benefits: small/very small improvement in pain relief, physical function, & sleep quality with the risk of AE.[mod-high certainty evidence]

Are Cannabinoids Safe?

Adverse effects (AE) are very common with cannabinoids. Approximately 8-9 patients out of 10 will develop an adverse effect to cannabinoid therapy and ~1 patient in 10 will stop therapy because of an adverse effect.[2] Notable AEs include feeling "high" **NNH=4**; sedation **NNH=5**; speech disorders **NNH=5**; dizziness **NNH=5**; and ataxia/muscle twitching **NNH=6**.[2] Additional concerns include driving impairment, addiction risk, euphoria, and psychosis. Some cannabinoids may be safer than others, but this is not well studied (including specific THC/CBD ratios). See next page. Option, but caution in older adults.[75] Cannabis use disorder is associated with self-harm & overdose death in youth.[74]

PERSPECTIVES ON Medical Cannabis

Cannabis is useful?

- *Some patients have tried a dozen or so standard medications without success, and now are trying, or want to try cannabis. If these patients find success with cannabis, and we help them do so safely, we will have done a great service for them.*
- *When patients say a medication helps, we should listen to them, just as we listen when patients tell us the antidepressant or anti-emetic we prescribed is helping.*
- *By developing products with a higher CBD-to-THC ratio, many tolerability concerns could be overcome.*
- *If cannabis helps our patients use less opioids, that's an attractive tradeoff.*
- *I plan to discuss what would constitute success, set realistic expectations, and conduct a trial over 4-12 weeks, after which any benefits vs harms will be assessed along with the decision on whether to continue or discontinue.*

Cannabis should be avoided?

- *Every other medication we prescribe has standard dosing and potency; no other medication is smoked. Inhaled cannabis contains 400+ compounds, and it's unclear which are important and how they interact. On top of that, each inhaled puff can be different from the last.*
- *There is no evidence that cannabis is superior to prescription cannabinoids; therefore regulated & approved prescription cannabinoids should always be preferred.*
- *In clinical trials, benefits are typically small and may just be a placebo effect. Meanwhile, adverse events are common. We have a professional duty to only prescribe medications when it can be done safely, and with cannabis the harms almost always outweigh the benefits. These harms may not be fully appreciated by patients.*
- *If we routinely authorize cannabis today, will it mirror the opioid crisis tomorrow?*

A final thought: *If a patient told you they were getting benefit from ibuprofen over-the-counter, you might recommend they continue taking it. You might even prescribe it. But would you feel the same way if the patient was using 6 grams of ibuprofen per day? Or if the patient insisted that the ibuprofen was improving their blood sugar control? Or if the patient had a history of GI bleeds?*

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. {Ask "Who is using? How are they using?, & Why…?"}
- **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%.[25] 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 an n=1 **trial with an exit strategy is important**. Not all patients will respond to, or function well on, these medications.

… Or Something Better?

If patients are wanting relief from pain – physical or emotional – there are often better choices! Non-pharmacological approaches to coping and living well with pain will be essential for success!

Misc info: **Synthetic illicit cannabinoids**: e.g. K2, Spice – highly potent CB1/CB2 receptor agonists; case reports of severe acute toxicity.[52] **Phytocannabinoid**: cannabinoid derived from cannabis (e.g. THC, CBD, & MANY 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 (link). **Concentrated Cannabis** e.g. hash, shatter, budder, wax: contains THC as high as 90%. **Dabbing**: vaping small amounts of concentrated cannabis. **Travelling with cannabis outside of Canada**: not recommended. **Non-medical cannabis**: aka "recreational". **Is cannabis opioid-sparing?**: Evidence is still unclear.[58-66]
Submitting AE to Health Canada: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/recalls-adverse-reactions-reporting/report-side-effects-cannabis-products.html 💻 (see for tips for cannabis products)

Cannabinoids: Comparison Chart

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Generic/TRADE	Indications & Comments	DOSING	$/30d	Adverse Events AE / Contraindications CI / Drug Interactions DI / Monitor M
Prescription Cannabinoids (pharmaceutical grade)				
Nabilone CESAMET, g PL synthetic THC analogue 0.5, 1mg cap ☎ ▼ ⌂ 0.25mg cap ✗ ▼ ⌂	Preferred over cannabis.[CFP'18] ✓ severe nausea/vomiting from cancer chemotherapy ✆ off-label: AIDS-related anorexia ☎ Palliative pain ✆ Neuropathic pain • Not detected in SK urine drug screen	**Initial**: 0.25-0.5mg po HS **Usual**: 1-2mg po daily-BID for CINV 1mg po BID for neuropathic pain **Usual max**: 6mg/day {Onset 60-90min; duration 8-12 hrs}	$23-36 g $252-494 g $252 g $736 g [$1390]	**AE: Some notes on adverse events:** • percentages below are often "worst case scenarios" from systematic reviews, yet due to trial-design issues could also be underestimates. • adverse events **dose-related** (↑dose =↑AE), & more common with THC products • 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).[44] **CBD** appears safer than THC, but some of its psychotropic effects are underappreciated (e.g. vs placebo in predominately pediatric trials: aggression/anger 3-5% vs <1%; irritability/agitation 5-9% vs 2%; somnolence 25% vs 8%).[31]
Nabiximols SATIVEX ✗ ⊗ PL extracted THC/CBD 2.7mg THC & 2.5mg CBD (plus terpenoids) per spray (peppermint flavour; poor taste) (contains alcohol) ❄ refrigerate prior to dispensing Not available in USA.	Preferred over cannabis.[CFP'18] ✓ advanced cancer pain (adjunctive) ✓ multiple sclerosis neuropathic pain or spasticity (adjunctive) • Spasticity may require lower doses than pain (e.g. 4-5 sprays vs >8 sprays per day). • Detected in SK urine drug screen	• Spray under the tongue or into side cheek (may alternate sides). • Shake vial gently. Device requires priming (3 sprays). **Initial**: 1 spray sublingually HS **Usual**: 1 spray sublingually q4h **Usual max**: 12 sprays per day {Onset 15-40min; duration 2-4 hrs}	3 vial pack = $673 ($2.50/spray) (90 spray/vial) $75 $468 $917	**drowsiness or sedation** up to 50% across cannabinoids.[2] **dizziness** up to 32% across cannabinoids.[2] **psychiatric disturbances** up to 17% across cannabinoids,[2] and up to 27% with inhaled cannabis,[COMPASS] including depression, anxiety, apathy, panic, paranoia, hallucination. In Colorado, accounts for ~25% of cannabis-related hospital visits.[Monte'19] **euphoria** up to 15%, and **feeling "high"** up to 35% across cannabinoids.[2] **acute psychosis or dissociation** up to 5% across cannabinoids.[2] **1st episode psychosis** daily cannabis ↑3x & THC ≥10% ↑5x vs never users.[Forti'19] **schizophrenia unmasking:** cannabis may hasten first psychotic episode by 2-6 yrs.[8] **speech disorders** up to 32%, and **ataxia** up to 30% across cannabinoids.[2] **impaired memory** up to 11%.[2] Also: **impaired cognitive performance** (~for up <28days) **irritability or agitation** up to 9%, and **anger or aggression** up to 5% with CBD.[31] **appetite changes:** decreased appetite in up to 22% of patients on CBD,[31] but conversely increased appetite in up to 38% of patients on dronabinol.[18] **GI issues:** dry mouth; diarrhea up to 20%, vomiting up to 15% with CBD.[19,31] Conversely, ↓ nausea in up to 20% of pts with dronabinol.[18] **SATIVEX**: mouth irritation. In Colorado, accounts for ~30% of cannabis-related hospital visits.[Monte'19] **cannabis hyperemesis syndrome:** severe abdominal pain/vomiting; requires drug discontinuation; relieved by hot shower; capsaicin to abdomen useful;[32] ?IV haloperidol **pneumonia** up to 8% with oral CBD.[31] **↑ LFTs** up to 16% of pts on CBD;[31] ?related to concomitant valproate/clobazam. **driving impairment:** risk of fatal car crash approximately doubles with THC.[28,55] **withdrawal** with abrupt discontinuation (see withdrawal symptoms on next pg) **red eyes** reported with non-medical use of oral and smoked THC. **rare or uncertain:** ?sexual problems, ?cancer testicular, ?↓BMD, ?pancreatitis.
Cannabidiol EPIDIOLEX PL extracted CBD 100mg/mL solution [FDA'18] (contains alcohol, sesame oil; strawberry flavour)	✓ Seizures: Lennox-Gastaut syndrome or Dravet syndrome in patients & Tuberous sclerosis complex [≥1 yrs] • Not detected in SK urine drug screen	**Seizures** (Lennox-Gastaut or Dravet): **≥1yrs**: 2.5-10mg/kg/dose po BID usually give before a meal • Food (fat/caloric): ↑ absorption.	**Not available in Canada**	
Dronabinol MARINOL PL synthetic THC **USA only**: 2.5, 5mg, 10 cap (in sesame oil) 5mg/mL solution **SYNDROS** (contains alcohol)	✓ severe nausea/vomiting from cancer chemotherapy ✓ AIDS-related anorexia	**Initial**: 2.5mg po HS **Usual**: 2.5-5mg po TID-QID for chemo nausea/vomiting (~5mg/m²) 2.5mg po BID ac lunch and supper for anorexia [AIDS 3] **Max**: 20mg/day	**D/C from Canadian market**	
Medical Cannabis (Plant)				
Oral Cannabis Oils ✗ ⊗ PL THC/CBD in various ratios, e.g.: 25mg THC / 0mg CBD per mL 1mg THC / 20mg CBD per mL 3mg THC / 3mg CBD capsule many other formulations & potencies available. **Veteran's Affairs**: coverage available for some patients	No official indication. May be medically authorized in Canada to any patient for any indication (i.e. "off-label use"). • THC detected in urine drug screen up to 4 weeks after last dose (esp. with chronic/heavy use) • **Oral vs inhaled**: Oral has lower bioavailability (~10% vs ~25%),[1] slower onset (30-60min vs 5-10min),[4] longer duration (4-8 hrs vs 2-4 hrs),[1] & does not have respiratory risk. • **Smoked vs vaped**: smoking speculated to have more respiratory risk (but data limited), but vaping has risk too (2,602 reports of vaping lung injury in US).[70,73] Vaping ~2x more potent (smoking destroys some drug via combustion). • **Vaping devices**: Consider a Health Canada approved vaporizer. **"Marijuana Math"** *note: estimate only – some uncertainty!* What is the estimated THC dose if **1 joint**, containing 0.5 grams of 10% THC dried cannabis, is smoked? **Answer**: 500mg cannabis x 10% THC x 50% loss to combustion ≈ **25mg THC**	**Initial**: CBD 2.5-5mg po daily-BID +/- THC 1-2.5mg po daily-BID (for pain) **Usual**: Uncertain due to lack of randomized trials. Titrate slowly, e.g. CBD q2-3d, THC q2-7d. (Consider titrating CBD to 40mg/day first, then adding THC if needed, with THC then titrated to max 40mg/day)[87] • Food increases absorption. • Consider 1st dose at 7 p.m. to leave time for assessing effect. • Consider weekend trial start (or when impairment less disastrous).	$7 e.g. 60mL bottle of oil containing 1200mg CBD ≈ $130 Use a calibrated dropper	**CI**: **pregnancy** ↓birth Wt & ↑preterm,[83] ?stillbirth, ?negative neurodevelopment; **breastfeeding**; <21-**25**yrs (CBD exception: tx-resistant seizures); psychosis/schizophrenia hx.[6] **Caution**: in elderly (↑AE),[82] **SUD history**, **driving** (sometimes contraindicated) <4-5hrs after inhalation/<6hrs after ingestion <8 hrs after euphoria (studies focused on THC component); hx of seizures, psychiatric disorders (e.g. bipolar, anxiety), CVD, or respiratory dx.[9] Caution: ped toxicity with edible ingestion. **DI: 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. **All cannabinoids**: additive CNS effects (e.g. sedation, confusion) with EtOH, BZDs, opioids, anticholinergics, anti-epileptics, etc. Avoid ≥ 3 CNS drugs.[BEERS'19] [?disulfiram-rxn if EtOH in product] Also consider additive effects: sympathomimetic, CNS, depressive, & anticholinergic. **THC-containing products** 2C9 & 3A4 substrate: ↓ levels by CBZ, SJW, phenytoin, etc. ↑ levels by clarithromycin, fluoxetine, fluvoxamine, gemfibrozil, etc. **CBD-containing products** 2C19 & 3A4 substrate: ↓ levels by CBZ, SJW, phenytoin, etc. ↑ levels by clarithromycin, fluconazole, fluoxetine, fluvoxamine, gemfibrozil, etc. 2C19 inhibitor: ↑ levels of citalopram/escitalopram, **clobazam**, warfarin; ?↑ levels of DOACs. ↓ levels of clopidogrel, ?additive hepatotoxicity risk with valproic acid or clobazam.[19,20] **Smoked cannabis**: smoking may result in 1A2 induction; e.g. ↓ levels of antipsychotics, caffeine, TCAs, theophylline, warfarin **Nabilone**: while a THC-mimic, does not have THC drug interactions. **M**: HR, BP, CNS adverse effects, psych symptoms, tx agreement, CUD, LFTs (with **EPIDIOLEX**)
Dried Cannabis ✗ ⊗ THC/CBD in various ratios, often to smoke/vape, e.g.: 12.5% THC 4% THC / 10% CBD 1% THC / 13% CBD many other potencies available. ❄ refrigerate for max stability **Veteran's Affairs:** coverage available for some patients **Trend:** toward ↑ potency products.[54] (e.g. 4% THC in 1995 → 12% in 2014; some may now be in the ~20% range) **Average joint**: ~0.3g dried cannabis.[69] **Medical use in USA**: 39 States & D.C. **Recreational use USA**: 21 States & D.C.		Guidelines recommend **avoiding** smoked cannabis.[2,7] **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.) **Usual**: Uncertain due to poor quality evidence. Titrate slowly. Based on market data for 2017 in Canada, patients taking cannabis for medical purposes titrated themselves to an average dose of **750mg** dried cannabis per day.[16]	In 2019 in Canada,[72] the average retail price was $10/g and the average street price was $6/g $12-24 for 1-2 puff HS $180 for 750mg/day $720 for 3g/day	

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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.[2] Conduct a trial over 4-12 wks; review benefit vs harm
  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 use disorder hx. For more details, see 💻 RxFiles Cannabis Q and A.

Prescribing/Authorizing Cannabinoids Safely

Cannabinoids are substances which may be misused or cause a substance use disorder; caution is needed when prescribing. In general, follow similar principles to prescribing opioids (see page 131-132). A summary of these principles is as follows:

☐ Optimize suitable non-cannabis therapies 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 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 (CUD)

☐ 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![67]

☐ Monitor for benefits & harms. **Exit Strategy**: stop (often taper) if trial unsuccessful.
Possible taper to prevent withdrawal: ↓ by 25% q1week.
Monitor more vigilantly in those at higher risk, esp where quality evidence/guidelines lacking.

Perioperative Resource: ASRA Pain Medicine Consensus Guidelines for the perioperative patient on cannabinoids.[86]

Monitoring for Cannabis Use Disorder (CUD)

9% of adults who use cannabis non-medically may develop addiction (adolescents are 2-4x more likely).[51,76,77,84]
Counselling Adolescents & Parents About Cannabis Infographic (CPS)

Prior to Tx: Screen for CUD

1) Options for Screening:

CUDIT-R
specific to cannabis.[45]

CAGE-AID Questionnaire
short & practical.[46]

2) Diagnosing: use DSM-5 criteria (listed in CFP Guidance document): has 11 components, 2 or more +'ve but exclude tolerance & withdrawal if taking for therapeutic purposes with medical supervision.[53]

{**4Cs of Addiction**: Craving, loss of Control, Compulsive use, Continued use despite harm}

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

In primary care,[47] watch for:

- ♦respiratory problems
- ♦depression/anxiety/amotivation
- ♦issues functioning/concentrating (e.g. in studies, work, relationships)
- ♦those at ↑risk of self-injury/harm (e.g. veterans - suicidality, seniors - AEs, DIs)

Treating CUD:[48-50]

a) Brief interventions
b) Withdrawal management (e.g. sleep hygiene, brief symptomatic relief, ?nicotine replacement)
c) Psychosocial interventions (e.g. motivational enhancement, CBT)

[Note: Pharmacologic tx, e.g. naltrexone, appears ineffective at this time] Cochrane'19

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.

CUD increased 3-4-fold over 20 years following legalization in Denmark.[80]

Choosing Between Products

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

	Prescription Cannabinoids e.g. nabilone, nabiximols	Cannabis	
		via medical authorization	via retail sale
Quality Control	Regulated. Health Canada pharmaceutical production standards in place (has Drug Identification Number).	In SK, 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.[43] However, similar to non-Rx herbal supplements, cannabis may have less vigorous production standards than Rx drugs. Products require standardized symbol: red stop-sign shape with cannabis leaf & "THC." Edibles must have child-resistant packaging.	
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).	Patient selects the product, dose, dosing interval, and route of administration. Difficult to provide monitoring, boundaries, or education.
	Note: despite prescriber attempts to guide product and dosing, patients may supplement with retail cannabis against medical advice.		
Access	Dispensed by community pharmacy.	Exclusively by mail/courier.	At cannabis retail store; online ordering possible too.
Paperwork	Written or electronic prescription.	See **Paperwork Required for Medical Cannabis** box, right.	None.
Coverage	• Occasional private insurance coverage. • SK EDS and prior approval criteria for specific indications.	• Occasional private insurance coverage (e.g. Manulife and Sunlife on a case-by-case basis as of 2018). • Veteran's affairs coverage (max 3g/day dried cannabis)	No coverage by any drug plans or private insurance; can't be claimed on income tax.
		~$8/gram; May grow at home to ↓costs. {Calculator for home production limit amount - link below}	Average price still uncertain (Ranges from $8-20/gram)

Paperwork Required for Medical Cannabis

1. Complete medical document form (link ❶). In SK, complete treatment agreement form (link ❷, or visit RxFiles.ca and search "agreement").[56]
2. Submit medical document to Licensed Producer (link ❸) 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 ❹).
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.

❶ www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/marihuana/info/med-eng.pdf
❷ http://www.cps.sk.ca/iMIS/Documents/Programs%20and%20Services/Patient%20Agreement%20Template%20-%20Medical%20Cannabis.pdf
❸ https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/industry-licensees-applicants/licensed-cultivators-processors-sellers.html
❹ www.canada.ca/en/health-canada/topics/production-cannabis-for-your-own-medical-purposes.html

People taking for medical purposes (vs non-medical)
- Use more frequently
- Use products other than dried flower & trend towards low THC/high CBD

Calculator for the production of a limited amount of cannabis for medical purposes: http://health.canada.ca/en/health-canada/services/drug-health-products/buying-using-drug-health-products-safely/cannabis-medical-purposes/accessing-cannabis-medical-purposes/production-cannabis-medical-purposes/calculator.html

☎=EDS in SK ✆=prior approval NIHB ✗ =not covered SK ⊗=not covered NIHB ⌂=NIHB palliative care **2-AG**=2-Arachidonoylglycerol **AEA**=Anandamide **CBD**=cannabidiol **CB1**=cannabinoid receptor type 1 **CB2**=cannabinoid receptor type 2 **CBZ**=carbamazepine **CINV**=chemotherapy-induced nausea and vomiting **CUD**=cannabis use disorder **MS**=multiple sclerosis **PIP**=pharmaceutical information program **TCA**=tricyclic antidepressant **SCI**=spinal cord injury **SJW**=St. John's Wort **THC**=delta-9-tetrahydrocannabinol

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Cannabinoids: Online Extras

College of Physicians & Surgeons of Saskatchewan: The College's bylaw

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. 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

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 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.

Submitting Adverse Effect information to Health Canada:
https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/recalls-adverse-reactions-reporting/report-side-effects-cannabis-products.html

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.

Cannabinoid	**137**
Cannabinoid Use Disorder	137
Cannabis	**137**
CBD	**137**
Marijuana	137
Medical Cannabis	137
Anorexia	138
Cannabidiol	138
Cannabinoid	**138**
Cannabis	**138**
CBD	**138**
CESAMET	**138**
Dried Cannabis	138
Dronabinol	138
EPIDIOLEX	138
Marijuana	138
MARINOL	138
Nabilone	**138**
Nabiximols	138
Oral Cannabis Oils	138
SATIVEX	138
Smoke	138
Smoked/vapourized Cannabis	138
Smoking	138
Tetranabinex/nabidiolex	138
THC	138

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