



### CANNABINOIDS - An Overview

Cannabis contains hundreds of compounds including ~70 cannabinoids. The most psychoactive cannabinoid is Delta-9-tetrahydrocannabinol (also known as dronabinol or THC). The other 2 less psychoactive cannabinoids are Delta-8-THC & cannabidiol (CBD) which may have analgesic & anti-inflammatory activity. Cannabinoid receptors (CB<sub>1</sub> & CB<sub>2</sub>) are where these agents work. General dosing considerations: start low & go slow.

#### Cannabinoid Comparisons:

Agent	Possible use	Side effects, <b>C</b> , <b>DI</b>	Dose	Cost 30d
<b>Dronabinol</b> <b>MARINOL</b> $\chi^{\otimes}$ -synthetic THC 2.5, 5 mg cap (sesame oil) <b>PL</b> -store in fridge	Treat severe <b>N&amp;V</b> from cancer chemo Treat AIDS related <b>anorexia</b> { Oral form – some abuse potential } Schedule III in USA, only II in Canada.	N&V, ataxia, confusion, coordination problems, dizziness, somnolence, vertigo, red eyes, $\uparrow$ or $\downarrow$ BP, palpitations, $\uparrow$ HR, flushing, panic rx, delusion of persecution, depersonalization, depression, disturbance in thinking & euphoria & still an <b>abuse</b> potential <b>C</b> : pregnant, breast feeding, ?Sz, psyc hx <b>DI</b> : $\uparrow$ SE: disulfiram, ethanol, fluoxetine, sleep meds. Theophylline <sup>theo</sup> level	2.5-5mg po TID-QID chemo N&V (~5mg/m <sup>2</sup> ) 2.5mg bid ac lunch & supper to $\uparrow$ appetite AIDS 3 <b>Start</b> 2.5mg po HS Max 20mg/d	\$202-500 \$137 \$72
<b>Marijuana</b> $\chi^{\otimes}$ (Banji, Cannabis sativa, Grass, Pot, Weed etc... Cost ~\$10-20/g) Contains: Delta-9-THC <b>PL</b> esp ♀ flowers & leaves ~10-20% THC, ?? pesticides present Delta-8-THC, cannabidiol & CBD {USA 2010: 14 states permit medical use}	An euphoriant. (recreational use) Possibly effective: $\uparrow$ appetite AIDS, $\downarrow$ pressure for glaucoma, MS neuropathic pain & tics <sup>20</sup> -see <b>Category 1</b> MMAR list below Unknown: dandruff, hemorrhoids, obesity, asthma, urinary infections, leprosy, preventing rejection after kidney transplants ... Sometimes used in <b>baking</b> for medicinal effect without risks of smoking.	Dry mouth, N&V, red eyes; heart, lung <sup>29</sup> & BP dx, $\downarrow$ mental fx, panic rx, $\uparrow$ weight & appetite, hallucinations, flashbacks, sedation; ?depression & sexual problems; ?cancer; gynecomastia ? $\uparrow$ steatosis with hepatitis C, ?psychosis <sup>62,73</sup> <b>C</b> : pregnant, breast feeding, ?seizures, ?psych hx ( $\uparrow$ periodontal disease) <b>DI</b> : $\uparrow$ SE: disulfiram, ethanol, fluoxetine, sleep meds. Theophylline <sup>theo</sup> level, warfarin? ♦potency/purity concern if unregulated ♦1 joint= $\leq$ 5 cigarettes from lung fx view <sup>29</sup>	1-3 grains (65-195mg) for smoking;  Hashish plant resin 1 grain (16-65mg) Rare: Lead adulteration to THC	Health Canada (~12.5%THC) \$5/gram 1-866-337-7705 Authorized producers & possession >2400 people approved Feb'08 -Dose as a proposed daily amount eg. $\leq$ 5g/day <sup>10</sup> {Ave 2.5g/day in pain}
<b>Nabilone</b> $\blacktriangledown$ <b>CESAMET</b> 0.5, 1mg cap (0.25mg) $\chi^{\blacktriangledown}$ <b>PL</b> (compound for low-dose e.g. simple syrup 5mg/50ml)	Treat severe <b>N&amp;V</b> from cancer chemo ⚠ EDS Sask.=nausea/anorexia in AIDS {Sleep benefit in small fibromyalgia trial} <sup>47 n=31</sup> { Oral form – some abuse potential } Schedule II in USA & in Canada. Not positive in urine drug screen!	Drowsiness, vertigo, psych high/euphoria, dry mouth, depression, ataxia, $\uparrow$ HR, $\downarrow$ BP, blurred vision, hallucinations, sedation, headache & still an abuse potential <b>C</b> : pregnant, breast feeding, ?Sz, psyc hx <b>DI</b> : $\uparrow$ SE: disulfiram, ethanol, fluoxetine, sleep meds. Theophylline <sup>theo</sup> level	1-2mg OD-BID for chemo N&V <b>Start</b> 0.25-0.5mg po HS $\uparrow$ by 0.5mg q2days Max 6mg/d	\$230-830 \$60-120
<b>Tetranabinex/nabidiolex</b> <sup>11</sup> <b>SATIVEX</b> $\chi^{\otimes}$ Buccal spray soln 5.5ml= ~51 sprays Natural extract contains: Delta-9-THC 2.7mg & CBD 2.5mg/spray peppermint flavor <b>PL</b>	<b>Adjunctive relief of advanced cancer pain; &amp; MS neuropathic pain/spasticity</b> <sup>pts &gt;18yr</sup> ♦ Trial n=66 <sup>5w</sup> aided approval for this indication <sup>18</sup> ; but product studied in 5 short trials with a total of 368 pts. ♦ Trial n=38 <sup>10wk</sup> in diabetic peripheral neuropathy; no better than placebo in pts with pain despite prior TCA tx. <sup>54</sup> Approved as a narcotic April05 with <b>CONDITIONS</b> (promising evidence must be further confirmed) Canada <b>first</b> country in the world to approve its use.	mouth irritation <sup>~20%</sup> , dizziness, $\uparrow$ HR, euphoric mood, changes in mood & concentration, drowsiness, bad taste, vertigo, reaction time <b>C</b> : allergy cannabinoids, propylene glycol, ethanol or peppermint oil, pts with severe heart, liver or kidney impairment, pregnant; ? psych hx <b>DI</b> : $\uparrow$ SE: disulfiram, ethanol, fluoxetine, sleep meds. Theophylline <sup>theo</sup> level; may $\uparrow$ levels of amitriptyline & fentanyl	Buccal 1 spray q4h directed below the tongue/or side cheek (often use 4 - 5 sprays/day for MS) (often use $\geq$ 8 sprays/day for cancer) Initial: 1 spray/day; $\uparrow$ q1-2d Max ~12 sprays/day Prime: 2-3 times initially Unopened: Refrigerate Room temp: stable for 28days Low dose: may spray into milk 	\$575 per 4 bottles (~200doses or ~40 days)

ac=before BP=blood pressure CBD=cannabidiol **C**=contraindication **DI**=drug interaction BP=blood pressure Dx=disease Fx=function HR=heart rate hx=history MS=multiple sclerosis N&V=nausea & vomiting Sz=seizures rx=reaction THC=delta-9-tetrahydrocannabinol  $\chi$  not Sask. formulary  $\otimes$  not NIHB  $\blacktriangledown$ =covered by NIHB ⚠=Exception Drug Status Sk ♀=female

#### Canadian Society of Addiction Medicine Statement: Oct, 1999

♦ "Cannabis is chemically classified in the **hallucinogen** category of psychoactive substances. The regular use of cannabis products is known to cause harmful health effects, including **addiction**, with its associated consequences to individuals, communities & society, among those that are susceptible. Currently, available scientific information and clinical practice experience indicate that overall, there is **more risk than benefit**, in the use of cannabis products for medicinal purposes. Ongoing well-designed clinical research into the possible medicinal uses of cannabis products is essential, using the same rigorous standards that are applied to any therapeutic agent prior to its introduction into general clinical practice."

#### Other issues to consider: (consider using CMPA release form [http://www.cmpa-acpm.ca/portal/cmpa\\_docs/english/content/issues/common/pdf/com\\_release\\_form\\_for\\_medical\\_practitioners-e.pdf](http://www.cmpa-acpm.ca/portal/cmpa_docs/english/content/issues/common/pdf/com_release_form_for_medical_practitioners-e.pdf))

- ♦ bill to **decriminalize** appears to be shelved until the next election (likely fines rather than criminal charges for possession but heavier penalties for grow-ops)
- ♦ Marijuana Medical Access Regulations (MMAR July/2001, Revised June/05)<sup>10</sup> defines specific circumstances for medical use of marijuana:  
**Category 1:** compassionate end-of-life care; pain/spasms from MS, spinal cord injury or disease; pain/cachexia/anorexia/weight loss/nausea from cancer or AIDS; pain from severe arthritis; or seizures from epilepsy {use **Form B1**}. Application by a medical practitioner (a GP or a specialist in the area of the condition)  
**Category 2:** other serious conditions {use **Form B2**}. A family doctor or specialist can sign the medical declaration. However an **assessment** of the case by a specialist is needed **if** the medical practitioner is not already a specialist for the patient's medical condition.

#### Broader Considerations:

- ♦ Pain → based on very limited evidence: no more effective than codeine,  $\uparrow$  side effects & **need larger trials**<sup>5</sup>  
 → cannabis is moderately efficacious for chronic pain, but benefit may be partially (or completely) offset by potentially serious harms.<sup>51,55</sup> limited evidence
- ♦ MS → modest therapeutic effect & risk of side effects thus **be cautious** about using cannabinoids<sup>7,8,9</sup>  
 {Small spasticity benefit & possible less disability & no major safety concerns in a 12 month CAMS MS trial n=502 follow up; pts felt these drugs helped their disease.}<sup>12</sup>

#### Limits of the Evidence:<sup>2-4, 9, 12, 47, 51</sup>

- ♦ limited RCT's, small short trials, differing routes, forms & types of cannabinoids makes assessing efficacy almost impossible

**Possible approach:** A close review of 1) the indications, 2) what meds were previously used & 3) the context of the "therapeutic trial" of marijuana. These people should have 4) a random urine screen & 5) an addictions assessment/addiction services, complete with 6) collateral information from family & others. Then 7) a focused case management discussion should be held, with all the assessors & care providers, before any decision is made. 8) Consider using "treatment agreement", structured approach for non-oral formulations. 9) Start low dose at HS to minimize side effects. {Consideration: **Fourth line** analgesic for the management of chronic neuropathic pain.}<sup>50</sup> Canadian Pain Society 2007

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Prepared by: Brent Jensen BSP, Loren Regier BSP BA for [www.RxFiles.ca](http://www.RxFiles.ca)

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Link to – Health Canada - Medical Marihuana: How to Apply: <http://www.hc-sc.gc.ca/dhp-mps/marihuana/how-comment/applicant-demandeur/index-eng.php>

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May/09 **CNN**: The average potency of marijuana, which has risen steadily for three decades, has **exceeded 10 percent** for the first time, the U.S. government will report on Thursday. Scientists working for the government predict that potency, as measured by the drug's concentration of the psychoactive ingredient THC, will continue to rise. At the University of Mississippi's Potency Monitoring Project, where thousands of samples of seized marijuana are tested every year, project director Mahmoud ElSohly said some samples have THC levels exceeding 30 percent. Average THC concentrations will continue to climb before leveling off at 15 percent or 16 percent in five to 10 years, ElSohly predicted. The average THC for tested marijuana during 2008 was 10.1 percent, according to the government, compared to 1983 when it was reportedly under 4 percent. Even drugs seized at the United States' southwest border are showing increasing potency, the Office of National Drug Control Policy says. The median potency increased from 4.8 percent in 2003 to 7.3 percent in 2007. Marijuana from Mexico and other southern sources traditionally had lower THC content than other sources. <http://www.whitehousedrugpolicy.gov/drugfact/marijuana/index.html>
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