PRESCRIBING CANNABINOIDS AND MEDICAL CANNABIS IN PRIMARY CARE Respectfully Submitted by Trudy Huyghebaert, PharmD (April 2018)

Towards Optimized Practice (TOP) has developed and published Clinical Practice Guidelines for Medical Cannabinoids in January 2018. These guidelines are based on the best available evidence to date regarding the use of Cannabinoids and are available on their website: http://topalbertadoctors.org/home/

The three main indications for prescribing cannabinoids based on available evidence are 1) Pain (neuropathic and palliative pain only); 2) Spasticity in MS or Spinal Cord Injury; 3) Chemotherapy induced nausea and vomiting.

There is a lack of reliable evidence for all other conditions and the harms in most cases outweigh the benefits. Further research is required in order to support its use in other conditions at this time.

In regard to chronic pain (neuropathic and palliative cancer pain), 9% of patients will experience at least a 30% reduction of their pain scores after 4 weeks of use. This equates to a number needed to treat (NNT) of 11 to benefit one patient. In terms of nausea and vomiting with chemotherapy, the number needed to treat is 3. However, it is important to note the number needed to harm (NNH) with cannabinoid therapy is 6.

Based on the available evidence for the above indications, Cannabinoids may be considered as a third line agent when at least two or more agents have been tried and has not resulted in adequate symptom control (pain or nausea/vomiting).

It is recommended when prescribing cannabinoids, we initially select a pharmaceutically prepared and standardized product licensed by Health Canada such as nabilone (Cesement[®]) or nabiximols (Sativex[®]). However, if it has been determined that the patient is to be prescribed medical cannabis (dried herb or CBD oils) we must follow the Standards of Practice provided by the College of Physicians and Surgeons of Alberta (CPSA) which requires the physician to register with the CPSA to be authorized to prescribe cannabis for medical purposes. Once authorized, the prescriber will then assess the patient and complete a medical document indicating patient information, prescriber information and cannabis use (daily quantity of dried cannabis in terms of grams per day and period of use, not longer than 1 year). This medical document to a Health Canada approved licensed dealer to obtain the medical cannabis prescription. There must be a follow up at least every three months once patient is stabilized.

Points to consider when prescribing medical cannabis (oils or dried marijuana)

- 1. It is difficult to standardize concentration of active ingredients and concentrations can have a wide range (5 to 27% of THC). Recommended maximum THC concentration is 9%.
- 2. Smoking marijuana has risks in terms of inhalation toxicity and long term consequences similar to smoking other products such as tobacco, especially in patients with underlying lung conditions.

Recommendations for operating dangerous equipment or performing potentially dangerous activities after use (i.e. driving):

- No driving for 3 to 4 hours after inhaled medical marijuana
- No driving 6 hours after oral medical marijuana
- No driving for at least 8 hours if a "high" was noted for any product.

Potential interactions with prescription medication

CNS depression: any medication that may result in CNS depression can have an unpredictable and potentially additive effect when Cannabinoids are used; this includes ETOH, opioids and benzodiazepines.

CVS: Anticholinergic medications can increase risk of tachycardia with cannabinoids; blood pressure lowering medications may enhance hypotensive effects of cannabinoids (also true for levodopa, duloxetine and PDE5 inhibitors such as sildenafil and tadalafil).

Please see article written by Joe Tabler on September 2017 newsletter regarding cardiovascular and cerebrovascular mortality and marijuana use.

	Cannabinoids	Control (Placebo unless indicated)	NNT (Number Needed to Treat)	GRADE quality of evidence	
Chronic Pain (median follow	-up 4 weeks)				
≥30% Reduction in Chronic (Neuropathic plus Cancer) Pain ^{††}	39%	30%	11	Very low	
≥30% Reduction in Neuropathic Pain	38%	30%	14	Very low	
≥30% Reduction in Palliative Pain	30%	23%	Not statistically significant (~15)**	Very low	
Change in Chronic Pain Scales (0-10) [†]	Baseline ~6 Decreased 1.2-1.6	Baseline ~6 Decreased 0.8	-	Very low	
Chemotherapy-Induced Nau	isea & Vomiting (medi	an follow-up 1 day)			
Control of Nausea and Vomiting (Cannabinoids vs. Placebo)	47%	13%	3	Moderate	
Control of Nausea and Vomiting (Cannabinoids vs. Neuroleptics)	31%	16% (versus neuroleptics)	7	Low	
Spasticity (median follow-up 6 weeks)					
Global Impression of Change	50%	35%	7	Low	
≥30% Improvement in Spasticity	35%	25%	10	Low	
Change in Spasticity (0- 10) [†]	Baseline ~ 6.2 Decreased 1.3-1.7	Baseline ~ 6.2 Decreased 1.0	-	Very low	

TABLE 1: Estimated benefit of Cannabinoids (From TOP CPG Cannabinoids, Jan 2018)

TYPE OF ADVERSE EVENT	CANNABINOID EVENT RATE	PLACEBO EVENT RATE	NUMBER NEEDED TO HARM
Overall	81%	62%	6
Withdrawal due to Adverse Events	11%	~3%	14
Serious Adverse Events	Not statistically significant		
Central Nervous System Effects	60%	27%	4
"Feeling High"	35%	3%	4
Sedation	50%	30%	5
Speech Disorders	32%	7%	5
Dizziness	32%	11%	5
Ataxia/Muscle Twitching	30%	11%	6
Numbness	21%	4%	6
Disturbance Attention/Disconnected Thought	17%	2%	7
Hypotension	25%	11%	8
Dysphoria	13%	0.3%	8
Psychiatric	17%	5%	9
Euphoria	15%	2%	9
Impaired Memory	11%	2%	12 [†]
Disorientation/Confusion	9%	2%	15
Blurred Vision/Visual Hallucination	6%	0%	17
Dissociation/Acute Psychosis	5%	0%	20

Table 2: Adverse Events reported in clinical trials:

Reference: http://topalbertadoctors.org/download/2238/Medical%20Cannabinoid%20CPG.pdf?_20180329165248

Medication	General Dosing Guidelines	Cost Per Month
medication		(generic costs where available)
Nabilone (Cesamet [®]) capsule	Start at 0.5 mg ghs and slowly titrate to 1 mg BID as	\$94 to 305 (for 2 to 6 mg/day) per month
0.25 - 1 mg (THC) depending on	tolerated. Max dose 6 mg/24 hours	
capsule strength		0.25 mg strength not covered
		0.5 mg capsule is \$0.77/cap**
		1 mg capsule is \$1.55/cap**
		**Covered by most plans, including
		Alberta Blue Cross
Nabiximols (Sativex [®])	Start at 1 spray q4h prn (max 4 sprays per day for	\$226 to \$903 (4 to 12 sprays per day) per
buccal spray	initiation), then increase as tolerated.	month
2.5 mg THC + 2.5 mg CBD	Usual dose is 5 sprays/day	Approximately \$3 to 5/spray
	Maximum dose 12 sprays/day (limited evidence for	*NOT covered by most plans, including
	doses above 12 sprays)	Alberta Blue Cross*
	*best evidence for spasticity in MS and spinal cord	
	injury*	
Medical Marijuana (Dried)	Start at 0.4 g per day (target dose in clinical trials)	\$250-750 per month
THC <0.5% to >27% CDB 0% to 9%	Titrate up to 1 to 2 g per day (approximately 2 to joints)	(based on 1 to 2g/day use)
		\$3-12 per gram (average \$8.37/g)
	** in Alberta, physicians must contact college if	
	prescribing cannabis and fill out Patient Medical	
	Document and send to CPSA within 1 week of	Available from Licensed Producers
	completion**	approved by Health Canada (List available
	Care Charden de Chardline france CDCA	from website:
	See Standard of Practice from CPSA	https://www.canada.ca/en/health-
	(http://www.upsa.ca/stanuaruspractice/cannabis-tor- medical-nurnoses/)	products/medical-use-
		marijuana/licensed-
		producers/authorized-licensed-
		producers-medical-purposes.html)

Table 3: Basic prescribing information for nabilone and nabiximols and medical marijuana (drie
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Table adapted from: http://strauss.ca/OEMAC/wp-content/uploads/2015/09/1.-Dr.-Daniel-Schecter-Cannabinoids-and-Occupational-Health.pdf



Standard of Practice Cannabis for Medical Purposes

Under Review: No Issued by Council: April 3, 2014 Reissued (name change only): May 3, 2017

Cannabis for Medical Purposes

The <u>Standards of Practice</u> of the College of Physicians & Surgeons of Alberta ('the College') are the <u>minimum</u> standards of professional behavior and ethical conduct expected of all regulated members registered in Alberta. Standards of Practice are enforceable under the *Health Professions Act* and will be referenced in the management of complaints and in discipline hearings. The College of Physicians & Surgeons of Alberta also provides <u>Advice to the Profession</u> to support the implementation of the Standards of Practice.

Health Canada has approved the use of cannabis for medical purposes. Physicians have the choice to treat or not to treat their patient's medical condition or symptom(s) with cannabis.

- (1) A physician who chooses not to treat patient's medical condition or symptom(s) with cannabis should do so in accordance with the <u>Code of Ethics</u> and <u>Conscientious Objection</u> standards of practice.
 - A physician who chooses to treat patients with cannabis must:
 - (a) register with the College as an authorizer of cannabis for medical purposes,
 - (b) attempt and find conventional therapies ineffective in treating the patient's medical condition or symptom(s),
 - (c) assess the patient's risk of addiction using a standard addiction risk tool,
 - (d) receive informed consent¹ in accordance with the Informed Consent standard of practice,
 - (e) review available prescription databases, including the Pharmacy Information Network (PIN) and the <u>Triplicate Prescription Program</u> (TPP) to obtain a patient medication profile,
 - (f) comply with provincial and federal regulations, including Health Canada's <u>Information for</u> <u>Health Care Professionals</u> and,
 - (g) complete a patient's medical document.

http://www.cpsa.ca/standardspractice/cannabis-for-medical-purposes/

The Patient's medical document must be faxed back to the CPSA within 1 week of completion. The patient must then seek out a Licensed Producer approved by Health Canada and list is available from their website. (<u>https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-use-marijuana/licensed-producers/authorized-licensed-producers-medical-purposes.html</u>)

(2)

References:

- 1. <u>http://www.ccic.net/picture/upload/File/ACE%20Resources/CCIC%20Patient%20Reference%20</u> <u>Card.pdf</u>
- 2. https://citiva.com/safety-and-benefits-of-cannabinoid-medicine/
- 3. <u>http://www.cpsa.ca/standardspractice/cannabis-for-medical-purposes/</u>
- 4. <u>https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-use-marijuana/licensed-producers/authorized-licensed-producers-medical-purposes.html</u>
- 5. <u>http://topalbertadoctors.org/home/</u>
- 6. <u>http://strauss.ca/OEMAC/wp-content/uploads/2015/09/1.-Dr.-Daniel-Schecter-Cannabinoids-and-Occupational-Health.pdf</u>