Utah Department of
Health & Human Services
Center for Medical Cannabis

Guidance on the suggested use of medical cannabis

Chronic pain

Disclaimer: In Utah, the qualifying condition of pain for medical cannabis is defined as pain lasting longer than two weeks. The term chronic pain, as generally used in medical literature, means pain lasting more than 3 to 6 months. We employ the term chronic pain in this document.

About this document: The following information on the use of medical cannabis serves as a suggested use guide for those participating in the Utah Medical Cannabis Program. The intended audience for this document includes, pharmacy medical providers, patients intending to use medical cannabis, and caregivers of patients intending to use medical cannabis.

This document details the guidance on the use of medical cannabis for chronic pain. This document does not include general instructions on the use of medical cannabis, contraindications, warnings, precautions and adverse reactions to using cannabis and drug-to-drug interactions which could be found in the extended guidance document titled *Guidance on the Suggested Use of Medical Cannabis.* The extended guidance document can be found on the Department of Health and Human Services Center for Medical Cannabis website (www.medicalcannabis.utah.gov).

About the authors: This document was authored by the Utah Cannabis Research Review Board and Department of Health and Human Services staff.

About the Utah Cannabis Research Review Board: Under Utah Health Code 26-61-201, the Cannabis Research Review Board is a board of medical research professionals and physicians who meet on a voluntary basis to review and discuss any available scientific research related to the human use of cannabis, cannabinoid product or an expanded cannabinoid product that was conducted under a study approved by an Institutional Review Board (IRB) or was conducted and approved by the federal government.

IMPORTANT NOTE: As always, in the event of significant side effects, stop use of medical cannabis until side effects have resolved, and then reduce to previous, best-tolerated dose. To avoid unwanted psychoactive side effects," start low and go slow" especially when using cannabis products for the first time or using new dosages or types of products.

There is moderate evidence to support the conclusion that medical cannabis and cannabinoids can have clinically significant beneficial effects in the management of persistent pain, particularly pain that is due to nerve damage or neuropathy. This is based on supportive findings from good to fair quality controlled clinical trials with very few opposing findings.

Smoking cannabis is not permitted under the Utah health code. Any mention of smoking in this document refers to the method used for a particular study and is stated for your information only. The Department of Health and Human Services, the Cannabis Research Review Board, and the State of Utah do not promote smoking as a method of cannabis use.

Chronic pain is the most common condition (87-94%) cited by individuals who are seeking to use cannabis for medical purposes (National Academies of Sciences, Engineering, and Medicine, 2017*a*). A meta-analysis (Whiting et al., 2015) of eight placebo-controlled trials involving 254 patients with chronic pain showed >30% reduction in pain in 37% of patients using cannabis or cannabinoids compared to 31% of patients getting placebo (OR, 1.41 [95% CI, 0.99-2.00]; eight trials). Seven of these eight trials used nabiximols, an oral mucosal spray with a 1:1 ratio of THC:CBD, and one trial using smoked inhaled cannabis. The single placebo-controlled trial in this review that used smoked cannabis (3.6% THC) looked at patients with pain due to HIV-associated peripheral neuropathy and showed an odds ratio for significant pain reduction of 3.43 (CI = 1.03-11.48) when compared with placebo (Abrams et al., 2007).

A 2021 systematic review conducted by the Pacific Northwest Evidence-based practice center, found insufficient or no evidence for benefits or risks for low THC, oral cannabidivarin, whole-plant THC (12% THC), all cannabinoids vs. non-placebo

comparators (McDonagh et al., 2021). The 2021 review found that cannabinoids, particularly those with high THC:CBD or equal THC:CBD, may improve some short-term pain outcomes, especially among people with neuropathic pain.

A 2015 systematic review looked at chronic peripheral neuropathic pain treated with inhaled forms of cannabis (smoked or vaporized flower) (Andreae et al., 2015). Underlying conditions included neuropathy due to HIV, trauma, spinal cord injury, diabetes mellitus, and complex regional pain syndrome. In this review meta- analysis of five randomized placebo-controlled trials performed in the USA involving a total of 178 middle-aged patients showed an odds ratio for significant pain relief (>30% reduction) of 3.22 (CI = 1.59 – 7.42) when compared with placebo and that inhaled cannabis appeared to provide significant short term relief from chronic neuropathic pain for one in 5-6 patients being treated.

A review on the use of smoked cannabis for the treatment of neuropathic pain suggested that the efficacy of smoked cannabis (NNT = 3.6, for a 30% reduction in pain) was comparable to that of traditional therapeutic agents (e.g. gabapentin, NNT = 3.8), slightly less than that observed with tricyclic antidepressants (NNT = 2.2), but better than lamotrigine (NNT = 5.4) and selective serotonin reuptake inhibitors (NNT = 6.7) (Grant, 2013). In this review, the concentrations of THC in smoked cannabis ranged between 2% and 9%, with an average concentration of 4% yielding good efficacy. Furthermore, the authors suggest that cannabis may present a reasonable alternative or adjunctive treatment for patients with severe, refractory painful peripheral neuropathy who have tried other therapeutic avenues without satisfactory results.

A 12-week blinded randomized placebo-controlled study from England (2012) involved 279 patients with stable multiple sclerosis (Zajicek et al., 2012). Active treatment (N= 144) was an oral extract from Cannabis sativa in soft gelatin capsules containing cannabidiol (range 0.8 -1.8 mg) and Δ9 THC (2.5mg). Treatment consisted of a starting dose of one capsule (2.5mg Δ9 THC) twice daily with a two- week dose titration phase and a ten-week maintenance phase. The total treatment duration was 12 weeks. Participants were assessed at two, four,

eight, and 12 weeks after the start of treatment. The maximum allowable total daily dose was 25mg Δ9 THC. By the end of the 12-week study, 46% of those receiving the active oral cannabis extract treatment had self-titrated to maximum dose of 25mg/day of Δ9 THC vs. 70% of the placebo group. The rate of relief from muscle stiffness and body pain after 12 weeks was almost twice as high with oral cannabis extract group than with the placebo (29.4% vs. 15.7%; OR 2.26; 95% CI 1.24 to 4.13; p=0.004). Adverse reactions were mild to moderate in intensity and were two times more frequent in the treatment group than the placebo group.

The 2017 report from the National Academies of Sciences Medicine and Engineering on the health effects of cannabis concludes that *"There is substantial evidence that cannabis is an effective treatment for chronic pain in adults"* (National Academies of Sciences, Engineering, and Medicine, 2017*b*). However, the authors of this report also cautiously note that only a handful of studies have evaluated the use of cannabis in the United States, and all of them evaluated cannabis in flower form provided by the National Institute on Drug Abuse. They also note that many of the cannabis products that are sold in state-regulated markets bear little resemblance to the products that are available for research at the federal level in the United States and that very little is known about the efficacy, dose, routes of administration, or side effects of commonly used and commercially available cannabis products in the United States.

In summary, most systematic reviews of controlled clinical trials using cannabis and cannabis-based medicines, support the conclusion that cannabis and cannabis- based medicines demonstrate a modest analgesic effect and provide an option for the treatment of chronic non-cancer pain - particularly chronic neuropathic pain that has not adequately responded to treatment attempts using FDA-approved conventional treatments and interventions (Health Canada, 2018).

General considerations for recommending medicinal cannabis in the treatment of chronic pain (adapted from MacCallum and Russo, 2018):

1. In some patients, oral preparations may be more helpful than vaporized

cannabis flower due to the longer duration of action of oral preparations and first-pass hepatic metabolism of orally ingested THC to 11-hydroxy THC (more potent than THC).

2. In patients using orally ingested cannabis-based medicines for treatment of pain, sublingual administration of medical cannabis extracts, vaporization of cannabis flower, or use of a medical cannabis vape pen can be utilized as add-on treatments for episodic exacerbations of symptoms.
3. CBD may attenuate THC side effects, which may be useful for daytime dosing, or when driving is required.
4. Medical cannabis patients, in contrast to recreational users, frequently use chemotypes with significant amounts of CBD and generally use the smallest amount of THC needed to get the greatest improvement in symptom control, function, and quality of life, with the fewest adverse events.
5. Data from blinded controlled clinical trials comparing various ratios of CBD:THC and therapeutic synergy (entourage effect) of various cannabis chemotypes and cultivars are lacking, but anecdotal reports and preclinical and observational data suggest that terpenoids and phytocannabinoids other than THC and CBD may have some pain-reducing and/or anti-inflammatory effects, and relative amounts of CBD may alter the effects and side-effects of THC (Russo, 2011). Because of this, changing ratios of CBD:THC or using a different chemotype or cultivar may result in improved outcomes in pain management with fewer side effects in the individual patient where N=1.
6. Management of pain using medical cannabis may follow a bell-shaped dose- response curve and escalation of doses of medical cannabis products past a certain amount may not always result in improved control of pain and in some cases may actually result in loss of therapeutic effect along with increased risk of adverse reactions (Portenoy et al., 2012).
7. THC tolerance may be abrogated via a drug vacation of at least 48 hours, preferably longer. Patients may then find that much lower doses provide symptomatic benefit equal to or better than previously experienced (see suggested regimen devised by Dustin Sulak, DO: https://healer.com/programs/strategies-for-non-psychoactive-cannabis-use

/).

8. Patients should keep a 'symptom inventory' chart indicating response or efficacy for each cannabis product for each symptom as an aid for qualified medical providers in determining treatment response to medical cannabis in follow up visits. (See Patient Tracking Journal at the end of this document).

Treatment suggestions for use of orally ingested extracts of Cannabis for Cannabis-naïve individuals with chronic pain (adapted from MacCallum and Russo, 2018):

1. Review currently-used prescription medications and check for drug-drug interactions between THC/CBD and any prescribed medications the individual is taking.
2. When treating chronic pain, consider beginning treatment with a chemotype containing both THC and CBD. Anecdotal reports from some experienced cannabis treatment providers suggest that a product with a 1:1 ratio of CBD:THC (chemotype II) or higher levels of CBD is a reasonable starting place with lower risk of adverse reactions.[1] However, based on other anecdotal reports, some individuals may do subjectively better with other CBD:THC ratios (CBD predominant chemotype III, or THC predominant chemotype I) or cultivars containing higher levels of other specific cannabinoids and/or terpenes.
3. Follow general dosing titration recommendations for orally-administered medical cannabis cited earlier in this document
4. Do not expect rapid onset of analgesia using orally-administered cannabis extracts. Orally-ingested THC is metabolized to 11-hydroxy THC during first-pass hepatic metabolism. 11-hydroxy THC is up to 5x more potent than THC and can cause significant intoxication and bothersome adverse reactions, especially in cannabis-naive individuals. Absorption of orally-administered medical cannabis products and the 11-hydroxylation process may take several hours and can be variable depending on bioavailability factors such as concurrent dietary intake. Start low and go

slow.

5. Absorption and bioavailability of orally-administered cannabis-based medicines are usually increased when taken with a fatty meal.
6. If treatment of acute exacerbations of chronic pain is desired, the use of sublingually administered cannabis extract or inhalation of vaporized flower or vaporized cannabis extract (vape pen) may be preferable to orally ingested (swallowed) cannabis extract due to relatively rapid onset of effects with these alternative treatment modalities. Follow the general dosing suggestions in this document for vaporization of herbal cannabis or use of a vape pen.

Patient tracking journal

The following medical cannabis logbook is for the patient or caregiver to utilize and keep track of the effects of medical cannabis use on underlying disease symptoms and the strains/hybrids that were used in between patient visits to the medical cannabis pharmacy or to his/her qualified medical provider.
It is requested that a patient or a caregiver presents this information to the medical cannabis pharmacy or the qualified medical provider to specifically convey information regarding the efficacy of the medical cannabis that was utilized.

This journal is completely optional to use. This journal can be useful to help a pharmacist, or the medical provider understand a patient's symptom levels.
Note: Not every symptom and its scale will apply to every patient. Every patient is unique and may have different symptoms in their treatment/therapy process.

Warning: Smoking medical cannabis is not permitted in the State of Utah.

Date	**Product description**	**Dosage**	**Method of consumption**	**Rate the level of pain or discomfort for any of the following that occurred (1 being mild and 10 being severe)**		**Post-use report (list any side effects and severity)**
				Before use	**After use**	
				Pain _____ Agitation _____ Sleep disturbance _____ Cachexia/weight loss _____ Nausea _____ Seizures _____ Muscle spasms _____	Pain _____ Agitation _____ Sleep disturbance _____ Cachexia/weight loss _____ Nausea _____ Seizures _____ Muscle spasms _____	
				Pain _____ Agitation _____ Sleep disturbance _____ Cachexia/weight loss _____ Nausea _____ Seizures _____ Muscle spasms _____	Pain _____ Agitation _____ Sleep disturbance _____ Cachexia/weight loss _____ Nausea _____ Seizures _____ Muscle spasms _____	

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				Pain _____ Agitation ________ Sleep disturbance _____ Cachexia/weight loss ____ Nausea ______ Seizures ______ Muscle spasms ______	Pain _____ Agitation ________ Sleep disturbance _____ Cachexia/weight loss ____ Nausea ______ Seizures ______ Muscle spasms _____	

References

1. Abrams, D. I., Jay, C. A., Shade, S. B., Vizoso, H., Reda, H., Press, S., … Petersen, K. L. (2007). Cannabis in painful HIV-associated sensory neuropathy: A randomized placebo-controlled trial. Neurology, 68(7), 515–521. doi: 10.1212/01.wnl.0000253187.66183.9c
2. Andreae, M. H., Carter, G. M., Shaparin, N., Suslov, K., Ellis, R. J., Ware, M. A., Sacks, H. S. (2015). Inhaled Cannabis for Chronic Neuropathic Pain: A Meta-analysis of Individual Patient Data. The Journal of Pain, 16(12), 1221– 1232. doi: 10.1016/j.jpain.2015.07.009
3. Grant, I. (2013). Medicinal Cannabis and Painful Sensory Neuropathy. AMA Journal of Ethics, 15(5), 466–469. doi: 10.1001/virtualmentor.2013.15.5.oped1-1305
4. Health Canada. (2018). Information for Health Care Professionals - Cannabis (marihuana, marijuana) and the cannabinoids. Retrieved from https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids-eng.pdf
5. Maccallum, C. A., & Russo, E. B. (2018). Practical considerations in medical cannabis administration and dosing. European Journal of Internal Medicine, 49, 12–19. doi: 10.1016/j.ejim.2018.01.004
6. McDonagh, M.S., Wagner, J., Ahmed, A.Y., Fu, R., Morasco, B., Kansagara, D., Chou, R. Living Systematic Review on Cannabis and Other Plant-Based Treatments for chronic Pain. Comparative effectiveness review no. 250. (prepared by Pacific Northwest Evidence-based Practice center under contract no. 75Q80120D00006.) AHRQ publication no. 21(22)-EHC036. Rockville, MD: Agency for Healthcare Research and Quality; October 2021. doi: https://doi.org/10.23970/AHRQEPCCER250
7. Portenoy, R. K., Ganae-Motan, E. D., Allende, S., Yanagihara, R., Shaiova, L., Weinstein, S., Fallon, M. T. (2012). Nabiximols for Opioid-Treated Cancer Patients With Poorly-Controlled Chronic Pain: A Randomized, Placebo- Controlled, Graded-Dose Trial. The Journal of Pain, 13(5), 438–449. doi:10.1016/j.jpain.2012.01.003
8. Russo, E. B. (2011). Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. British Journal of Pharmacology, 163(7), 1344–1364. doi: 10.1111/j.1476-5381.2011.01238.x

9. The National Academies of Sciences, Engineering, and Medicine. (2017a). The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. (Ch. 4-1). Doi: https://doi.org/10.17226/24625
10. The National Academies of Sciences, Engineering, and Medicine. (2017b). The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. doi:https://doi.org/10.17226/24625
11. Whiting, P. F., Wolff, R. F., Deshpande, S., Nisio, M. D., Duffy, S., Hernandez, A. V., Kleijnen, J. (2015). Cannabinoids for Medical Use. Jama, 313(24), 2456. doi: 10.1001/jama.2015.6358
12. Zajicek, J. P., Hobart, J. C., Slade, A., Barnes, D., & Mattison, P. G. (2012). MUltiple Sclerosis and Extract of Cannabis: results of the MUSEC trial. Journal of Neurology, Neurosurgery & Psychiatry, 83(11), 1125–1132. doi:10.1136/jnnp-2012-302468

DISCLAIMER

The following information on the use of medical cannabis serves as a suggested use guide for those participating in the Utah Medical Cannabis Program. This document has been vetted and approved by the Utah Cannabis Research Review Board under Utah Health Code 26-61-202.

This document summarizes available peer-reviewed literature concerning potential therapeutic uses and harmful effects of cannabis and cannabinoids. With the ongoing nature of cannabis and cannabinoid research, it is not meant to be complete or comprehensive. It should be used as a limited complement to other reliable sources of information. This document is not a systematic review or meta-analysis of the literature and has not rigorously evaluated the quality and weight of the available evidence. There is a lack of controlled clinical trials yielding high-level evidence of predictable therapeutic benefits for any given condition other than those for FDA-approved formulations. This document includes warnings and risks related to the use of cannabis, including cannabis use disorder, potentially irreversible brain damage/mental illness, legal liability for driving under the influence (DUI), and potential for adverse work-related consequences.

All patrons participating in the Utah Medical Cannabis Program are advised to use this document and any such document produced from this original document as informational and educational. The use of medical cannabis is at one's own risk. **Medical cannabis is NOT a first-line therapy for most medical conditions.**

The information in this document is intended to help as far as available data allows Utah healthcare decision-makers, healthcare professionals, health systems leaders, and Utah Medical Cannabis patients to make well-informed decisions and thereby improve the quality of healthcare outcomes in patients using medical cannabis use. While patients and others may access this document, it is made available for informational purposes only, and no representations or warranties are made concerning its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or for applying clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process.

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