Utah Department of Health

Guidance on the Suggested Use of Medical Cannabis

Post-Traumatic Stress Disorder (PTSD)

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 qualified medical providers, 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 Utah Department of Health Center for Medical Cannabis website (www.medicalcannabis.utah.gov).

About the authors: This document was authored by the Utah Cannabinoid Product Board and Utah Department of Health staff.

About the Utah Cannabinoid Product Board: Under Utah Health Code 26-61-201, the Cannabinoid Product 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.

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 Cannabinoid Product Board under Utah Health Code 26-61-202.

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

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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 insufficient evidence to support the conclusion that medical cannabis or cannabinoids are effective or ineffective treatments for PTSD or symptoms of PTSD.

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PTSD may be caused by exposure to actual or threatened death, serious injury, or sexual violence, by directly experiencing traumatic event(s), or witnessing in person the event(s) as it/they occurred to others. Conventional treatments for PTSD usually include psychotherapy along with optional use of prescription medications to help manage ongoing and emerging symptoms while undergoing therapy. Cannabis has been anecdotally reported to be useful in managing anxiety, sleep disturbances, nightmares, and other symptoms in individuals suffering from PTSD. There are several pre-clinical observations involving the endocannabinoid system and CB1 receptor density in certain areas of the brain in individuals with PTSD (Neurmeister et al., 2015 & Neurmeister et al., 2013) that lend credence to a hypothesis that cannabis and cannabinoids could have some effect on symptoms of PTSD. However there is currently significant clinical uncertainty regarding the potential benefits, and also the possible harms of using cannabis or cannabinoids as treatment for PTSD or symptoms of PTSD. Several systematic reviews of this topic are outlined below:

1. A systematic review was conducted and reported in Annals of Internal Medicine in 2017 that looked at systematic reviews, clinical controlled trials, and observational studies with control groups that reported PTSD symptoms with and without the use of plant-based cannabis, and adverse effects of plant-based cannabis (O'Neil et al., 2017). Two systematic reviews, 3 observational studies, and no randomized trials were found. This review reported insufficient evidence to draw conclusions about benefits and harms, and the observational studies found that compared with non-use [of cannabis], cannabis did not reduce PTSD symptoms. Authors reported that the clinical trials reviewed had medium and high risk of bias, and overall evidence was judged insufficient to draw any conclusions regarding benefit or harms of using plant-based cannabis as treatment for PTSD.
2. A systematic review regarding medicinal use of cannabis was reported in 2017 by a team at the Portland, Oregon Veterans Hospital as part of treatment policy development effort by the VA system (Kansagara et al., 2017). One of the questions addressed in this review is, *"What are the effects of cannabis on health outcomes and healthcare utilization for adults who have PTSD?"* They found insufficient evidence examining the effects of

cannabis in patients with PTSD with no blinded controlled studies. They reported 2 observational studies with untreated controls that showed that cannabis use was not associated with improved outcomes in either study when compared to untreated controls.

3. The 2017 report on *The Health Effects of Cannabis and Cannabinoids (The National Academies of Sciences, Engineering and Medicine, 2017)* was unable to identify any good or fair-quality systematic review that reported on medical cannabis as an effective treatment for PTSD symptoms and determined that there was only one fair-quality small double-blind placebo controlled study that looked at nabilone (a synthetic cannabinoid) and found it to be helpful in managing symptoms of PTSD.
4. A literature review published in *Depression and Anxiety* in February, 2017 regarding treatment of PTSD using cannabis (Steenkamp et al., 2017) concluded that treatment outcome studies of whole plant cannabis and related cannabinoid effects on PTSD are limited and not methodologically rigorous, precluding conclusions about their potential therapeutic effects. The authors raised the concern that cannabis use has been linked to adverse psychiatric outcomes, including conditions commonly comorbid with PTSD such as depression, anxiety, psychosis, and substance misuse. They also noted that cannabis use is associated with worse treatment outcomes in PTSD naturalistic studies, and with maladaptive coping styles that may maintain PTSD symptoms. Their ultimate conclusion was that known risks of cannabis use currently outweigh unknown benefits of cannabis for treatment of PTSD.

There is currently no placebo-controlled trial data to guide or recommend the use of medical cannabis or cannabinoids as first-line agents in the treatment of PTSD or comorbid symptoms. Some anecdotal reports and observational studies suggest possible short-term benefits in some individuals with PTSD (Greer et al., 2014; Betthauser et al., 2015 & Roitman et al., 2014) but there are also longitudinal 10-year data in 2276 US veterans that demonstrate worse outcomes in individuals using cannabis to treat PTSD, including worse outcomes in PTSD symptom severity, increase in violent behaviors, and increase in measures of alcohol and drug use (Wilkinson et al., 2015). Cross-sectional studies have found a direct correlation between more severe PTSD symptomatology and increased motivation to use cannabis for coping purposes, especially among patients with difficulties in emotional regulation or stress intolerance (Bonn-Miller et al., 2007). These uncertainties and sometimes contradictory observations need to be addressed with robust randomized placebo-controlled clinical trials. Of note, there are currently at least two randomized trials and 6 other studies examining outcomes of cannabis use in patients with PTSD that are ongoing and are expected to be completed within 3 years.

Because of the current lack of randomized blinded placebo-controlled clinical trials, and current very significant clinical uncertainty regarding risks and benefits of medical cannabis in the treatment of PTSD, the use of medical cannabis to treat PTSD should generally be considered only if:

1. The diagnosis of PTSD has been made or confirmed by a board-certified psychiatrist or a PhD-level therapist with a degree in psychology or social work, or a psychiatric APRN (required by Utah Code 26-61a-104), and;
2. The individual with PTSD has not tolerated or adequately responded to robust clinical attempts using traditional treatment interventions including psychotherapy, and FDA-approved pharmacologic interventions, and;

3. The individual fully understands the known and potential unknown risks of using cannabis or cannabinoids to manage symptoms of PTSD including the potential for worse PTSD treatment outcomes, and;
4. The individual and qualified healthcare provider working together have arrived at the conclusion that the potential risks of using medical cannabis to treat PTSD may be justified by the possible benefits and potential for avoidance of assessed risks of continuing on with unmanaged symptoms of severe PTSD despite robust attempts using traditional interventions.

References

1. Betthauser, K., Pilz, J., & Vollmer, L. E. (2015). Use and effects of cannabinoids in military veterans with posttraumatic stress disorder. American Journal of Health-System Pharmacy, 72(15), 1279–1284. doi: 10.2146/ajhp140523
2. Bonn-Miller, M. O., Vujanovic, A. A., Feldner, M. T., Bernstein, A., & Zvolensky, M. J. (2007). Posttraumatic stress symptom severity predicts marijuana use coping motives among traumatic event-exposed marijuana users. Journal of Traumatic Stress, 20(4), 577–586. doi: 10.1002/jts.20243
3. Greer, G. R., Grob, C. S., & Halberstadt, A. L. (2014). PTSD Symptom Reports of Patients Evaluated for the New Mexico Medical Cannabis Program. Journal of Psychoactive Drugs, 46(1), 73–77. doi: 10.1080/02791072.2013.873843
4. Kansagara, D., O'Neil, M., Nugent, S., Freeman, M., Low, A., Kondo, K., … Morasco, B. (2017). Benefits and Harms of Cannabis in Chronic Pain or Post-traumatic Stress Disorder: A Systematic Review. Department of Veterans Affairs.
5. Neumeister, A., Normandin, M. D., Pietrzak, R. H., Piomelli, D., Zheng, M. Q., Gujarro-Anton, A., … Huang, Y. (2013). Elevated brain cannabinoid CB1 receptor availability in post-traumatic stress disorder: a positron emission tomography study. Molecular Psychiatry, 18(9), 1034–1040. doi: 10.1038/mp.2013.61
6. Neumeister, A., Seidel, J., Ragen, B. J., & Pietrzak, R. H. (2015). Translational evidence for a role of endocannabinoids in the etiology and treatment of posttraumatic stress disorder. Psychoneuroendocrinology, 51, 577–584. doi: 10.1016/j.psyneuen.2014.10.012
7. O'neil, M. E., Nugent, S. M., Morasco, B. J., Freeman, M., Low, A., Kondo, K., … Kansagara, D. (2017). Benefits and Harms of Plant-Based Cannabis for Posttraumatic Stress Disorder. Annals of Internal Medicine, 167(5), 332. doi: 10.7326/m17-0477
8. Roitman, P., Mechoulam, R., Cooper-Kazaz, R., & Shalev, A. (2014). Preliminary, Open-Label, Pilot Study of Add-On Oral Δ9-Tetrahydrocannabinol in Chronic Post-Traumatic Stress Disorder. Clinical Drug Investigation, 34(8), 587–591. doi: 10.1007/s40261-014-0212-3
9. Steenkamp, M. M., Blessing, E. M., Galatzer-Levy, I. R., Hollahan, L. C., & Anderson, W. T. (2017). Marijuana and other cannabinoids as a treatment for posttraumatic stress disorder: A literature review. Depression and Anxiety, 34(3), 207–216. doi: 10.1002/da.22596
10. The National Academies of Sciences, Engineering, and Medicine. (2017). The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. doi: https://doi.org/10.17226/24625
11. Wilkinson, S. T., Stefanovics, E., & Rosenheck, R. A. (2015). Marijuana Use Is Associated With Worse Outcomes in Symptom Severity and Violent Behavior in Patients With Posttraumatic Stress Disorder. The Journal of Clinical Psychiatry, 76(09), 1174–1180. doi: 10.4088/jcp.14m09475