

Guidance on the suggested use of medical cannabis

Persistent and debilitating muscle spasms

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 persistent and debilitating muscle spasms. 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 26B-1-420, 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.

Persistent and debilitating muscle spasms may result from a variety of distinct clinical conditions in adult and pediatric patients.

There is <u>limited evidence</u> to support the conclusion that cannabis or cannabinoids (oral cannabinoids, vaporized cannabis, or nabiximols) are an effective treatment for spasticity in adults with spinal cord injury, amyotrophic lateral sclerosis, or primary lateral sclerosis.

There is <u>insufficient evidence</u> to support the conclusion that cannabis or cannabinoids (nabiximols) are an effective treatment for spasticity in adults who have had a stroke

There is <u>insufficient evidence</u> to support the conclusion that cannabis or cannabinoids (CBD rich oil or nabiximols) are an effective treatment for spasticity children with traumatic brain injury or cerebral palsy.

^a Developed using level of evidence categories from the 2017 National Academies of Sciences, Engineering, and Medicine report on cannabis (National Academies of Sciences, Engineering, and Medicine, 2017*d*).

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Persistent and debilitating muscle spasms¹ may result from a variety of distinct clinical conditions in adult and pediatric patients such as spinal cord injury (SCI)/spinal cord disease (SCD), amyotrophic lateral sclerosis (ALS), primary lateral sclerosis (PLS), traumatic brain injury (TBI), stroke, and cerebral palsy (CP) among others. Guidance for use of medical cannabis in treating multiple sclerosis is detailed separately.

The terms muscle spasms and spasticity are not always used consistently in medical literature. Spasticity is an increase in muscle tone that worsens with movement resulting from upper motor neuron dysfunction.^{2,3} The term spasm is less specific and may be used by patients and providers to describe painful cramps, spasticity, clonus, dystonia, or other conditions.⁴

Spasticity is often assessed using the clinician-administered modified Ashworth scale (mAS), which grades symptoms on a 6-point scale from 0 (no abnormally increased muscle tone) to 4 (muscle is rigid in flexion or extension), or the originator 5-point Ashworth scale (AS). The mAS updated the AS by adding a "1+" intermediary score that is halfway between 1 and 2 on the AS scale.⁵ Decreases by at least 1 point on the mAS are estimated to be clinically meaningful to patients.⁶ Patient-reported spasticity assessed per numeric rating scales (NRSs) or visual rating scales (VRSs) are other common spasticity outcome measures.⁷

In animal models of MS spasticity, agonism of cannabinoid type 1 (CB₁) receptors improves spasticity.⁸It has been proposed that cannabinoids, particularly delta-9-tetrahydrocannabinol (THC), could improve spasticity by reducing excitatory glutamatergic neurotransmission.^{8,9} Nabiximols (Sativex), an oromucosal spray of cannabis plant extract containing an approximately 1:1 mixture of THC and cannabidiol (CBD), has received regulatory approval for treatment-resistant spasticity in adults with MS in many countries other than the United States.^{9,10}

Non-cannabinoid pharmacologic options for symptomatic management of spasticity include oral agents (eg, baclofen, tizanidine, benzodiazepines, dantrolene), intrathecal baclofen, and botulinum neurotoxin A injection.¹¹ According to experts, use of these therapies is limited by adverse effects and tolerance.⁸

The following summarizes clinical efficacy evidence from recent systematic reviews (SRs), primarily of randomized controlled trials (RCTs), for treatment of spasms with cannabis-based therapies.

• Spasticity from SCI/SCD:

Six unclear to high risk-of-bias or poor to fair quality trials (only assessed for 4 trials)^{6,26,27} demonstrated mixed efficacy of cannabinoids or cannabis (oral nabilone, dronabinol, or THC; oromucosal nabiximols; vaporized cannabis; or rectal THC-HS) for reducing spasticity in the short-term among patients with SCI/SCD, many of whom were paraplegic or quadriplegic (neurological injury

level was not reported by all trials).^{12-17,25}

If only results from the 4 trials who selected patients for spasticity at baseline are considered, spasticity was significantly reduced compared to placebo for at least 1 outcome measure in 3 of 4 trials.¹²⁻¹⁵ Spasticity was significantly improved in 1 of the 2 other trials of patients with pain at baseline (albeit not until 7 hours after the first dose, and only for the lower cannabis dosage),¹⁶ and spasticity on the modified Ashworth scale improved numerically with nabiximols compared to placebo in the other trial.¹⁷ There is uncertainty about findings from the trials due to potential bias, confounding, and small sample sizes.

• ALS or PLS

A randomized controlled trial with a low risk-of-bias met its primary outcome, showing that nabiximols significantly reduced mean spasticity scores on the mAS (calculated as a sum of multiple muscle groups) compared to placebo at 6 weeks (adjusted mean difference: -0.32 [95%CI -0.57 to -0.07]). Change on the Patient's Global Impression of Change (but not Neurologists' or Caregivers') scale also significantly favored nabiximols over placebo.¹⁸ There is some uncertainty due to the small sample size and evidence being limited to a single trial.

• Stroke

o In a small, randomized, cross-over, triple-blinded pilot trial, nabiximols did not significantly improve mean spasticity on a numerical rating scale from baseline to 4 weeks compared to placebo among adults who had a stroke and low pain at baseline. The co-primary outcomes of change in stretch reflexes per electromyographic recordings also did not improve with nabiximols compared to placebo. While no formal risk-of-bias assessment by a systematic review was performed for this trial, we note there is an unclear risk-of-bias arising from randomization (sufficient detail not reported) and attrition during the trial (only 83% of patients completed the trial). There is uncertainty due to the small sample size, the possible lack of statistical power (no power calculation was performed since it was a pilot trial), and bias.¹⁹

• Children with CP or TBI

o Two experimental trials primarily among children with CP found conflicting results for the treatment of spasticity with cannabis. Nabiximols did not significantly reduce mean spasticity scores from baseline to 12 weeks on a caregiver reported scale compared to placebo in a randomized controlled trial with some risk-of-bias concerns (Fairhurst et al 2020)²⁶; changes from

baseline in secondary outcome spasticity measures also did not differ from placebo.²⁰ In contrast, in the second trial with poorly reported methods and an unclear risk-of-bias (Libzon et al 2018),²⁹ CBD rich oil at 2 different dosages improved caregiver-reported spasticity at 5 months compared to baseline.²¹ Both trials were small, and the trial by Libzon et al carries uncertainty due to bias from the unknown randomization and blinding methods, confounding, and the lack of a placebo comparator.

Nearly all experimental trials studied cannabis-based treatments as an adjunct to other therapies (eg, skeletal muscle relaxants like baclofen and/or physical therapy).^{12,14-16,18-21} Only one trial that included patients with SCI tapered off other treatments before starting oral THC or rectal THC-HS during the trial.¹³

Trials used a variety of cannabinoid products including oral nabilone (N=1),¹² oral dronabinol or THC (N=3),¹³⁻¹⁵ oromucosal nabiximols spray (N=4),¹⁷⁻²⁰ CBD-rich cannabis oil (N=1),²¹ rectal THC-HS (N=1),¹³ and inhaled cannabis (N=1).¹⁶

Safety Concerns

Cannabinoid product tolerability and the degree of safety details reported varied between trials. In the 4 trials that administered patient-titrated oromucosal nabiximols, nabiximols generally had an acceptable safety and tolerability profile, with an expected increased incidence of mild to moderate adverse events (e.g., nausea, dizziness, somnolence, asthenia, vertigo) compared to placebo.¹⁷⁻²⁰ While nabiximols was tolerated by medically complex children in the trial by Fairhurst et al in general, some children considered the nabiximols formulation to be unpalatable; 12.8% of children in the nabiximols arm reported retching compared to 0% in the placebo arm.²⁰ Moreover, while evidence is limited, children with CP/TBI might be more susceptible to neuropsychiatric events with nabiximols compared to adults with MS, stroke, and ALS/PLS who received nabiximols in clinical trials. Three pediatric patients experienced hallucinations while receiving nabiximols, which led to a suicide attempt in one instance.²⁰ Another trial (Libzon et al) that enrolled children compared two oral CBD-enriched oils with a 6:1 or 20:1 CBD: THC ratio, and considered CBD-based oils to be well-tolerated and safe for up to 5 months. The clarity of AE reporting by Libzon et al was poor, but it is described that AEs among the 25 included children were limited to 2 events of worsened seizures (possibly attributable to underlying conditions or changes to anti-seizure medications), 2 events of behavioral changes, and 1 event of somnolence.²¹ In the

Fairhurst et al trial, serious AEs of seizures occurred in 2 patients (7.4%) in the nabiximols arm and 1 patient (4%) in the placebo arm.²⁰

Oral THC/dronabinol, rectal THC-HS, or nabilone were studied in 4 trials of adults with SCI: most of these trials poorly reported safety information. Few severe AEs occurred with nabilone, and common AEs associated with nabilone included drowsiness, asthenia, and mild vertigo.¹² In 2 trials that used high oral THC doses (range 10-15 to 60 mg daily), THC was generally associated with fatigue, increased or decreased anger, dry mouth, anxiety, and dysphoria.^{13,14} A high proportion of patients who received oral THC in one trial (23%) reported increased pain, which led to 80% of affected patients (4 of 5) discontinuing the oral THC.¹³ The final trial studied 2 doses of vaporized cannabis among patients with SCI and reported little detail about AEs.¹⁶ Patients who used vaporized cannabis did not discontinue the treatment due to AEs and no serious AEs occurred; 1 patient experienced temporary syncope that resolved without sequelae.¹⁶

An association between cannabis exposure and stroke, primarily ischemic, has been reported among people with or without other stroke risk factors in observational and descriptive studies.^{30,31} One included small, short-term RCT studied nabiximols oromucosal spray among older adults (median age of 68 years) with a history of a stroke, including ischemic stroke in 62% of people who completed the trial. Enrolled patients passed cardiovascular screening (blood pressure, electrocardiogram, and echocardiogram) at baseline.¹⁹ No adverse effects on blood pressure or heart rate were observed after 4 weeks of treatment, nor did any ischemic or hemorrhagic events occur among the population with a median of 4.2 years since their stroke.²⁸

Summary, Limitations, and Suggestions

In summary, it is our opinion that evidence for treatment of *spasticity* with cannabis or cannabinoids could be considered *limited* for adults with SCI or ALS/PLS, and *insufficient* for adults who had a stroke, and children with TBI or CP.

Available experimental evidence is limited to *short-term treatment* with CBPs, ranging from 1 day to about 20 weeks with a median of 6 weeks across the 10 trials.

Cannabinoid use may cause sedation, dizziness, or other neurologic adverse effects.We suggest that providers assess potential risks from sedation or dizziness before starting cannabis and provide appropriate counseling and clinical monitoring to mitigate risks. Follow general dosing guidance for cannabis, including starting at a low dose and up-titrating slowly.

For dosing guidance for treatment of persistent or debilitating muscle spasms, please refer to the general dosing suggestions at the beginning of the document titled Guidance on the Suggested Use of Medical Cannabis found on the Department of Health and Human Services Center for Medical Cannabis website (www.medicalcannabis.utah.gov).

References

1. Cannabinoid Research and Medical Cannabis § 203, 26B Utah Code Ann. ch. 4 § 2023 (2023). Accessed October 20, 2023. Available at https://le.utah.gov/xcode/Title26B/Chapter4/26B-4-s203.html?v=C26B-4-S203_2023050320230503

2. Rivelis Y, Zafar N, K M. Spasticity *StatPearls*. StatPeals Publishing; 2023. Accessed October 20, 2023. Available at <u>https://www.ncbi.nlm.nih.gov/books/NBK507869/</u>

3. Nielsen JB, Crone C, Hultborn H. The spinal pathophysiology of spasticity--from a basic science point of view. *Acta Physiol (Oxf)*. 2007;189(2):171-180. doi:10.1111/j.1748-1716.2006.01652.x

4. Pilitsis JG, Khazen O. Spasticity. 2023. Accessed October 20, 2023. Available at https://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Spasticity

5. Harb A, Kishner S. Modified Ashworth Scale. *StatPearls*. StatPearls; 2023. Accessed October 20, 2023. Available at <u>https://www.ncbi.nlm.nih.gov/books/NBK554572/</u>

6. Nabata KJ, Tse EK, Nightingale TE, et al. The Therapeutic Potential and Usage Patterns of Cannabinoids in People with Spinal Cord Injuries: A Systematic Review. *Current neuropharmacology*. 2021;19(3):402-432.

doi:<u>https://dx.doi.org/10.2174/1570159X18666200420085712</u>

7. Joseph D, Schulze J. Cannabinoid activity—is there a causal connection to spasmolysis in clinical studies? *Biomolecules*. 2021;11(6)doi:10.3390/biom11060826

8. Nielsen S, Murnion B, Campbell G, Young H, Hall W. Cannabinoids for the treatment of spasticity. *Dev Med Child Neurol*. 2019;61(6):631-638. doi:10.1111/dmcn.14165

9. GW Pharma Ltd. Sativex Oromucosal Spray. N02BG10. Electronic Medicines Compendium; 2022. Last Updated April 28, 2022. Accessed February 12, 2024. Available at https://www.medicines.org.uk/emc/product/602/smpc#gref

10. Carod-Artal FJ, Adjamian P, Vila Silván C, Bagul M, Gasperini C. A systematic review of European regional and national guidelines: a focus on the recommended use of nabiximols in the management of spasticity in multiple sclerosis. *Expert Rev Neurother*. 2022;22(6):499-511. doi:10.1080/14737175.2022.2075263

11. Chang E, Ghosh N, Yanni D, Lee S, Alexandru D, Mozaffar T. A Review of Spasticity Treatments: Pharmacological and Interventional Approaches. *Crit Rev Phys Rehabil Med*. 2013;25(1-2):11-22. doi:10.1615/CritRevPhysRehabilMed.2013007945

12. Pooyania S, Ethans K, Szturm T, Casey A, Perry D. A randomized, double-blinded, crossover pilot study assessing the effect of nabilone on spasticity in persons with spinal cord injury. *Arch Phys Med Rehabil.* 2010;91(5):703-707. doi:10.1016/j.apmr.2009.12.025

13. Hagenbach U, Luz S, Ghafoor N, et al. The treatment of spasticity with Delta9tetrahydrocannabinol in persons with spinal cord injury. *Spinal Cord*. 2007;45(8):551-562. doi:10.1038/sj.sc.310198218 14. Kogel RW, Johnson PB, Chintam R, Robinson CJ, Nemchausky BA. Treatment of Spasticity in Spinal Cord Injury with Dronabinol, a Tetrahydrocannabinol Derivative. *Am J Ther*. 1995;2(10):799-805. doi:10.1097/00045391-199510000-00012

15. Maurer M, Henn V, Dittrich A, Hofmann A. Delta-9-tetrahydrocannabinol shows antispastic and analgesic effects in a single case double-blind trial. *Eur Arch Psychiatry Clin Neurosci*. 1990;240(1):1-4. doi:10.1007/bf02190083

16. Wilsey B, Marcotte TD, Deutsch R, Zhao H, Prasad H, Phan A. An Exploratory Human Laboratory Experiment Evaluating Vaporized Cannabis in the Treatment of Neuropathic Pain From Spinal Cord Injury and Disease. *J Pain*. 2016;17(9):982-1000. doi:10.1016/j.jpain.2016.05.010

17. Jazz Pharmaceuticals. A Study of Cannabis Based Medicine Extracts and Placebo in Patients witth Pain Due to Spinal Cord Injury NCT01606202. ClinicalTrials.gov; 2012. Last Updated January 1, 2023. Accessed January 16, 2024. Available at https://clinicaltrials.gov/study/NCT01606202

18. Riva N, Mora G, Sorarù G, et al. Safety and efficacy of nabiximols on spasticity symptoms in patients with motor neuron disease (CANALS): a multicentre, double-blind, randomised, placebo-controlled, phase 2 trial. *Lancet Neurol*. 2019;18(2):155-164. doi:10.1016/s1474-4422(18)30406-x

19. Marinelli L, Puce L, Mori L, et al. Cannabinoid Effect and Safety in Spasticity Following Stroke: A Double-Blind Randomized Placebo-Controlled Study. *Frontiers in neurology*. 2022;13:892165. doi:<u>https://dx.doi.org/10.3389/fneur.2022.892165</u>

20. Fairhurst C, Kumar R, Checketts D, Tayo B, Turner S. Efficacy and safety of nabiximols cannabinoid medicine for paediatric spasticity in cerebral palsy or traumatic brain injury: a randomized controlled trial. *Dev Med Child Neurol*. 2020;62(9):1031-1039. doi:10.1111/dmcn.14548

21. Libzon S, Schleider LB, Saban N, et al. Medical Cannabis for Pediatric Moderate to Severe Complex Motor Disorders. *J Child Neurol*. 2018;33(9):565-571. doi:10.1177/0883073818773028

22. Wade DT, Robson P, House H, Makela P, Aram J. A preliminary controlled study to determine whether whole-plant cannabis extracts can improve intractable neurogenic symptoms. *Clin Rehabil*. 2003;17(1):21-29. doi:10.1191/0269215503cr581oa

23. Hansen JS, Gustavsen S, Roshanisefat H, et al. Cannabis-Based Medicine for Neuropathic Pain and Spasticity-A Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial. *Pharmaceuticals* 2023;16(8)doi:<u>https://dx.doi.org/10.3390/ph16081079</u>Accessed 20230728//. Available at

24. Berman J, Bosworth T, Guy G, Stott C, Group SSCIS. Sativex in the treatment of central neuropathic pain due to spinal cord injury: a randomised controlled study. Paper presented at: British Pain Society Annual Scientific Meeting; 2007, 2007. Available at http://www.epistemonikos.org/documents/4d90170bdce96be9e9e9c18e8b5aa0f435665b40

25. Wissel J, Haydn T, Müller J, et al. Low dose treatment with the synthetic cannabinoid Nabilone significantly reduces spasticity-related pain : a double-blind placebo-controlled cross-over trial. *J Neurol*. 2006;253(10):1337-1341. doi:10.1007/s00415-006-0218-8

26. Bilbao A, Spanagel R. Medical cannabinoids: a pharmacology-based systematic review and meta analysis for all relevant medical indications. *BMC medicine*. 2022;20(1):259. doi:<u>https://dx.doi.org/10.1186/s12916-022-02459-1</u>

27. National Institute for Health and Care Excellence. *Cannabis-based medicinal products. Evidence review for spasticity.* . NG144. NICE; 2019: 224 pages. Last Updated November 2019. Accessed October 27, 2023. Available at https://www.nice.org.uk/guidance/ng144/evidence/c-spasticity pdf-6963831760

28. Rosa GM, Puce L, Mori L, et al. Nabiximols effect on blood pressure and heart rate in post-stroke patients of a randomized controlled study. *Frontiers in cardiovascular medicine*. 2022;9:990188. doi:<u>https://dx.doi.org/10.3389/fcvm.2022.990188</u>

29. Ayala L, Winter S, Byrne R, et al. Assessments and Interventions for Spasticity in Infants With or at High Risk for Cerebral Palsy: A Systematic Review. *Pediatric neurology*. 2021;118:72-90. doi:<u>https://dx.doi.org/10.1016/j.pediatrneurol.2020.10.014</u>

30. Swetlik C, Migdady I, Hasan LZ, Buletko AB, Price C, Cho S-M. Cannabis Use and Stroke: Does a Risk Exist? *Journal of addiction medicine*. 2022;16(2):208-215. doi:https://dx.doi.org/10.1097/ADM.0000000000870

31. Gómez Ochoa SA. Stroke and cannabis use in patients with no cardiovascular risk factors: a systematic review of case reports. *Neurologia*. 2021;36(3):222-228. doi:10.1016/j.nrl.2017.09.016

32. Harb A, Kishner S. *Modified Asthworth Scale*. Treasure Island (FL): StatPearls Publishing; 2023. Accessed March 7, 2024. Available at <u>https://www.ncbi.nlm.nih.gov/books/NBK554572/</u>

33. Fleuren JFM, Voerman GE, Erren-Wolters CV, et al. Stop using the Ashworth Scale for the assessment of spasticity. *Journal of Neurology, Neurosurgery & amp; amp; Psychiatry*. 2010;81(1):46. doi:10.1136/jnnp.2009.177071 http://innp.bmj.com/content/81/1/46.abstract

34. Allan GM, Ramji J, Perry D, et al. Simplified guideline for prescribing medical cannabinoids in primary care. *Can Fam Physician*. 2018;64(2):111-120.

35. Utah Cannabis Research Review Board. *Guidance on the suggested use of medical cannabis. Multiple sclerosis.* . Services UDoHaH; 2023: 11 pages. Last Updated October 10, 2023. Accessed March 24, 2024. Available at <u>https://medicalcannabis.utah.gov/wp-content/uploads/Final-draft</u> <u>Multiple-Sclerosis_Approved.docx.pdf</u>

36. National Academies of Sciences Engineering and Medicine. *The Health Effects of Cannabis and Cannabinoids: the Current State of Evidence and Recommendations for Research* 2017: 486 pages. doi:<u>https://doi.org/10.17226/24625</u> Accessed March 22, 2024. Available at https://doi.org/10.17226/24625 Accessed March 22, 2024. Available at https://nap.nationalacademies.org/catalog/24625/the-health-effects-of-cannabis-and cannabinoids-the-current-state

37. McMaster University Health Information Research Unit. Search filters for Medline in Ovid syntax and the PubMed translation. hiru.mcmaster.ca; 2016. Last Updated February 9, 2016. Accessed November 7, 2022. Available at

https://hiru.mcmaster.ca/hiru/hiru_hedges_medline_strategies.aspx

38. Lefebvre C, Manheimer E, Glanville J. Searching for studies. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0.* The Cochrane Collaboration; 2011:chap 6. Accessed November 7, 2022. Available at https://handbook-5-1.cochrane.org/

39. Weber M, Goldman B, Truniger S. Tetrahydrocannabinol (THC) for cramps in amyotrophic lateral sclerosis: a randomised, double-blind crossover trial. *J Neurol Neurosurg Psychiatry*. 2010;81(10):1135-1140. doi:10.1136/jnnp.2009.200642

40. Zloto O, Weisman A, Avisar I, et al. Medical cannabis oil for benign essential blepharospasm: a prospective, randomized controlled pilot study. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 2022;260(5):1707-1712. doi:10.1007/s00417-021-05533-1

41. Silkiss RZ, Koppinger J, Truong T, Gibson D, Tyler C. Cannabidiol as an Adjunct to Botulinum Toxin in Blepharospasm - A Randomized Pilot Study. *Translational vision science & technology*. 2023;12(8):17. doi:10.1167/tvst.12.8.17

42. López-Sendón Moreno JL, García Caldentey J, Trigo Cubillo P, et al. A double-blind, randomized, cross-over, placebo-controlled, pilot trial with Sativex in Huntington's disease. *J Neurol*. 2016;263(7):1390-1400. doi:10.1007/s00415-016-8145-9

43. Fox SH, Kellett M, Moore AP, Crossman AR, Brotchie JM. Randomised, double-blind, placebo controlled trial to assess the potential of cannabinoid receptor stimulation in the treatment of dystonia. *Mov Disord*. 2002;17(1):145-149. doi:10.1002/mds.1280

44. Paulson A, Vargus-Adams J. Overview of Four Functional Classification Systems Commonly Used in Cerebral Palsy. *Children (Basel)*. 2017;4(4)doi:10.3390/children4040030

45. National Institute of Health. Study Quality Assessment Tools. 2021. Last Updated July 2021. Accessed February 26, 2024. Available at <u>https://www.nhlbi.nih.gov/health-topics/study</u> <u>guality-assessment-tools</u>

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 26B-1-420.

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 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 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.**

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