Medical Cannabidiol Petition Subcommittee Report

Prepared for the Medical Cannabidiol Board meeting on June 16, 2019

The Medical Cannabidiol Petition Subcommittee is charged with the review petitions for new conditions, review submitted literature, research additional literature, provide additional literature to the full Board and make a recommendation on the petition to the full Board. This document contains the Subcommittee's recommendations to the Full Medical Cannabidiol Board. The petitions that the Subcommittee considered for this meeting are as follows: 1. PTSD, Refractory to Standard Treatment

2. Generalized Anxiety Disorder
3. Tourette Syndrome
4. Any rare condition or disease that affects less than 200,000 individuals in the U.S., as defined in federal law, refractory to conventional treatment

The information below is a summary of the Subcommittees recommendations for each petition.

1. PTSD, Refractory to Standard Treatment

a. Vote: 3-0 to recommend rejection to the Iowa Medical Cannabidiol Board

Rationale: Evidence considered included references from the medical literature provided by:

a) the petitioner
b) search of UptoDate, searching "PTSD and cannabis", "treatment of PTSD"
c) search of Pubmed, searching "PTSD and cannabis", PTSD and THC", "PTSD and marijuana"; both unfiltered and filtered for "Reviews"

The majority of individual studies are either in lab or on animals. Those reporting patient clinical results are virtually all observational/un-controlled; usually with small numbers and short duration. Authors routinely criticize their own results and call for ". . .randomized, placebo-controlled trials (RCTs) of sufficient power and duration to confirm the findings our study suggests". Such RCTs do not appear in the searchable literature. Review articles universally recommend awaiting further evidence and withholding treatment with cannabis, with emphasis on lack of guidelines for indications/dosing and particularly on absence of any long term safety data. Both the Veterans Administration and the World Health Organization advise against use of cannabis.

Two significant RCTs of sufficient power and perhaps duration are underway which may be transformative but results not yet available. They can be reviewed at:

- https://clinicaltrials.gov/ct2/show/NCT02759185?term=PTSD+cannabis&rank=1
- https://clinicaltrials.gov/ct2/show/NCT02517424?term=PTSD+cannabis&rank=2

At the same meeting Dr. Miller moved that the full board approve PTSD for compassionate reasons because of the lack of good current therapy for PTSD and the high

risk of suicide with the condition. It did pass on a split vote, but with the following restrictions:

a) The 4.5gm cap on 90 day supply is the maximum unless the treating provider documents the need for higher amounts.
b) This approval is only for adults (defined as 18 years old and above).

The rational for these restrictions are:

a) There is not good scientific data to support the use of CBD/THC and until there is the amount of the potentially more harmful THC needs to be limited.
b) There is a growing body of evidence about the harm caused to developing brains in children from THC.

HF2589 was pending the Governor's approval so the Board took no further action on this petition. HF2589 was signed by the Governor and approved "post-traumatic stress disorder" as an adverse medical condition without specific restrictions.

2. Generalized Anxiety Disorder

a. Vote:

- The subcommittee (Liesveld, Richards, Shreck) voted unanimously to recommend denying the petition to add generalized anxiety disorder to the list of debilitating medical conditions for which the medical use of cannabidiol would be medically beneficial.

b. Rationale:

- The subcommittee reviewed the references forwarded by the GAD petitioner. Refer to attachments from Dr. Shreck's June 2, 2020 e-mail for the original documents.
- The 2015 Blessing article "Cannabidiol as a Potential Treatment for Anxiety Disorders" concludes that CBD has efficacy in reducing anxiety behaviors relevant to multiple disorders, including…..GAD…with a notable lack of anxiogenic effects. Preclinical and human findings have mostly involved acute CBD dosing in healthy subjects. It was concluded that it is currently unknown if chronic dosing of CBD in clinical populations has similar effects, and further study of CBD in the treatment of anxiety disorders was recommended.
- The 2012 Tambaro et al article reviews numerous aspects of both natural and synthetic cannabinoids including the pharmaceutical properties. The authors conclude that further studies are needed, and no recommendations were made for using cannabinoids for the treatment of anxiety disorders.
- Dr. Stoner's June 2017 review of the effects of marijuana on anxiety disorders concluded that pure CBD appears to decrease anxiety at all doses that have been tested, and pure THC appears to decrease anxiety at lower doses and increase anxiety at higher doses. concluded that "using marijuana to cope with anxiety may offer some short-term benefit, but well-controlled studies indicate that use of marijuana is associated with increased likelihood of substance use disorders."
- In addition to the above references, a Pubmed search found no new convincing

evidence supporting the use of cannabinoids to treat GAD since the Iowa Medical Cannabidiol Board denied a similar petition in August 2019. This includes a systematic review and meta-analysis on "Cannabinoids for the treatment of mental disorders" in The Lancet Psychiatry, Volume 6, Issue 12, pages 995-1010, December 1, 2019. The review concluded that "there is scarce evidence to suggest that cannabinoids improve….anxiety disorders…"

3. Tourette Syndrome

a. Vote:

- The Cannabidiol Study Subcommittee voted unanimously, 3-0, to deny this petition.

b. Rationale:

- *Additional supplementary literature and rationale attached*
- The published medical literature on medical cannabis and Tourette's is virtually all anecdotal reports of single patients or a small group. There are two placebo-controlled RCTs utilizing THC, one a single dose study and one extending over six weeks. Both reported statistically significant reductions in tics. Both were small numbers, adults only, included no follow-up or long-term safety data and did not address CBD.
- UpToDate is silent regarding cannabis in its Tourette's chapters on treatment. ・ Petitioner appealed to a retrospective observational study of a subset of Tourette's patients who self-identified as cannabis users, apparently using street drug, a majority of whom claimed their cannabis use reduced their tics and compulsive tendencies. No dosage, duration, or safety information included. ・ Petitioner appealed to the patient-driven Tourette's Association of America (TAA) website. It includes a pamphlet for primary-care-providers advising them on treatment of Tourette's—it is silent on cannabis use.
- Moreover, the TAA convened a panel of clinicians and researchers who: "…evaluated the currently available research and data on the safety and efficacy of medical marijuana and cannabis-based medicines, and have advised us that due to the lack of randomized, large scale, placebo-controlled clinical studies, scientific evidence is insufficient to reach a conclusion on the safety and/or the efficacy of medical marijuana for the treatment of Tourette Syndrome and Tic Disorders. In the absence of conclusive medical research, they are especially concerned about medical marijuana in the treatment ofchildren and adolescents. The Tourette Association of America shares that concern." This statement is on the TAA website.
- Finally, a large fraction of Tourette's care is pediatric and emerging data on brain development through age 25 was a factor in this decision.

4. Any rare condition or disease that affects less than 200,000 individuals in the U.S., as defined in federal law, refractory to conventional treatment

a. Vote:

- The Cannabidiol Study Subcommittee voted unanimously, 3-0, to deny this petition.

b. Rationale:

- *Additional supplementary literature and rationale attached*
- “Orphan Drug” legislation and subsequent designation of hundreds of thousands of diagnoses as “orphans” provided federal financial and regulatory relief designed to encourage pharmaceutical firms to study treatments for which they would never be compensated by standard market measures.
- Nothing in this legislation excused any developed treatment from passing FDA standards of efficacy and safety rendering this legislation irrelevant to this issue. ・ That the Iowa Medical Cannabidiol Board has included compassionate considerations in making recommendations on occasional specific diagnoses is not generalizable to the whole world of medicine. Each diagnosis must be considered individually and on its own merits."