

From: noreply@pharmacy.ohio.gov
To: MedicalMarijuana@med.ohio.gov
Subject: Condition Petition for Jeff Orlando
Date: Wednesday, November 20, 2019 12:09:15 PM
Attachments: [Question 5.pdf](#)

This message was sent from the Condition page on medicalmarijuana.ohio.gov.

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Specific Disease or Condition:
Generalized Anxiety Disorder

Information from experts who specialize in the disease or condition.

Medications for Anxiety include Benzodiazepines which work on the gaba receptors of the brain <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4020178/> CB1 Cannabinoid Receptors Regulate GABA Release <https://www.jneurosci.org/content/19/11/4544.short>

Relevant medical or scientific evidence pertaining to the disease or condition.

According to DSM-5 The key features of generalized anxiety disorder are persistent and excessive anxiety and worry about various domains, including work and school performance, that the individual finds difficult to control. In addition, the individual experiences physical symptoms, including restlessness or feeling keyed up or on edge; being easily fatigued; difficulty concentrating or mind going blank; irritability; muscle tension; and sleep disturbance.

Consideration of whether conventional medical therapies are insufficient to treat or alleviate the disease or condition.

Anxiety is commonly treated with benzodiazepines a drug that can have fatal withdrawals. It is also known to cause or exacerbate the ringing in ear -tinnitus. It can be addictive and there becomes a tolerance over time which leads to higher dosages prescribed and a dependence.

Evidence supporting the use of medical marijuana to treat or alleviate the disease or condition, including journal articles, peer-reviewed studies, and other types of medical or scientific documentation.

<https://www.ncbi.nlm.nih.gov/pubmed/23307069> <https://doi.org/10.1016/j.jad.2018.04.054>
<https://www.ncbi.nlm.nih.gov/pubmed/22729452>

Letters of support provided by physicians with knowledge of the disease or condition. This may include a letter provided by the physician treating the petitioner, if applicable.

Letter attached

- Question 5.pdf



SUBJECT MATTER EXPERT REPORT: CHRONIC/GENERALIZED ANXIETY DISORDER

PETITION OVERVIEW

MATERIALS SUBMITTED	DESCRIPTION
4731-32-05 (E)(3) <i>[The board shall consult with one or more experts who specialize in the disease or condition:]</i>	Solomon Zaraa, DO szaraa@compassionatecleveland.com Compassionate Cleveland 23250 Chagrin Blvd; Suite 310 Beachwood, OH, 44122 (216) 586-2606
4731-32-05 (C)(1)	Original petition "0108 - Rosenberger – Generalized Anxiety Disorder (trade secret).pdf" submitted on 12/31/2018 by Thomas Rosenberger Rosenberger@nciaohio.org Original petition "110 – McIntyre – Chronic Anxiety Disorder.pdf" submitted on 12/31/2018 by Dawn McIntyre dawnm@sistersoflotus.com
4731-32-05 (C)(2)	"Chronic/Generalized Anxiety Disorder"
4731-32-05 (C)(3) <i>[Information from experts who specialize in the study of the disease or condition:]</i>	Refer to: Expert Summary (below) Expert Conclusion (below) Expert Report (below)
4731-32-05 (C)(4) <i>[Relevant medical or scientific evidence pertaining to the disease or condition:]</i>	Refer to: Expert Report (below) References (below)
4731-32-05 (C)(5) <i>[Consideration of whether conventional medical therapies are insufficient to treat or alleviate the disease or condition:]</i>	Refer to: Expert Report (below) <i>Also refer to original petitions:</i> <i>"0108 - Rosenberger – Generalized Anxiety Disorder (trade secret).pdf"</i> <i>"110 – McIntyre – Chronic Anxiety Disorder.pdf"</i>
4731-32-05 (C)(6) <i>[Evidence supporting the use of medical marijuana to treat or alleviate the disease or</i>	Refer to: References (below)

condition, including journal articles, peer-reviewed studies, and other types of medical or scientific documentation:]

4731-32-05 (C)(7)

[Letters of support provided by physicians with knowledge of the disease or condition. This may include a letter provided by the physician treating the petitioner, if applicable]

Refer to:

“0108 - Rosenberger – Generalized Anxiety Disorder (trade secret).pdf”

“110 – McIntyre – Chronic Anxiety Disorder.pdf”

APPLICABLE STATUTES & RULES

PURSUANT TO OAC 4731-32-05, THE SUBJECT MATTER EXPERT SHALL REVIEW THE ABOVE-REFERENCED MATERIALS AND ISSUE A WRITTEN OPINION REGARDING THE CURRENT TREATMENT MODALITIES FOR THE PROPOSED DISEASE OR CONDITION AND WHETHER A MEDICAL MARIJUANA RECOMMENDATION COULD BE BENEFICIAL TO THE PROPOSED DISEASE OR CONDITION.

SUMMARY OF PROPOSED DISEASE OR CONDITION

[THE SUBJECT MATTER EXPERT WILL PROVIDE A BRIEF SUMMARY OF THE PROPOSED DISEASE OR CONDITION AND ITS CURRENT TREATMENT MODALITIES]

Anxiety disorders are one of the most prevalent mental health conditions with a point prevalence of up to 13% of the population and a lifetime prevalence of up to 28%. Anxiety disorders are implicated in negative work productivity and economic loss, health issues, and substance use. Current treatment standards for anxiety disorders include counseling/therapy or medications, followed by a combination of both if response is inadequate. However, nearly half of people who undergo all conventional treatments do not experience adequate therapeutic response. Furthermore, conventional prescription treatments are associated with risk of suicide, fatal overdose, or fatal withdrawal.

CONCLUSIONS REGARDING MEDICAL MARIJUANA

The following is my expert opinion to a reasonable degree of medical certainty regarding the applicability of recommending medical marijuana for the proposed disease or condition:

It is my expert opinion to a reasonable degree of medical certainty that Medical Marijuana, as defined by the Ohio Medical Marijuana Control Program, *has evidence* for safety, tolerability, and efficacy in the treatment of Chronic/Generalized Anxiety Disorder.

Therefore, *I recommend* that Chronic/Generalized Anxiety Disorder be considered as a qualifying condition for treatment with medical marijuana in the state of Ohio.

There is robust preclinical data and some clinical data regarding the effectiveness of cannabis or cannabinoids for the treatment of anxiety. Large-scale patient surveys identify improvement in core anxiety symptoms and reduction in potentially risky prescription medications. Most clinical data reports efficacy of moderate-dose CBD or THC/CBD combinations in treating anxiety. Research suggests that THC may have benefit at lower doses but not higher doses. There is conclusive clinical evidence from multiple randomized placebo-controlled trials regarding the safety and tolerability of high dose cannabidiol in children and adults with severe neurologic or psychiatric disorders.

If applicable, here are the strains and/or dosages that may be appropriate when using medical marijuana for the proposed disease or condition:

- Oral:
 - Based on a randomized placebo controlled trial, use of oral THC is well tolerated in adults at 7.5mg or below per dose. However, benefits of THC were not present at 12.5mg per dose.
 - 1:1 ratios of THC:CBD appear to be most effective with good tolerability.
 - Treatment with CBD alone requires high dosing (up to 10mg/kg in adults) that may cause potential risk of elevated liver enzymes.
 - Synergistic effect of CBD and THC improves efficacy.
 - CBD's antagonism of CB1 sensitivity reduces side effects with higher doses of THC.
- Inhaled:
 - Large patient surveys report effective management of anxiety symptoms with inhaled cannabis. Dose ranges are well within the Ohio Medical Marijuana Control Program's daily limits. (Lucas 2019).
 - 1:1 ratios of THC:CBD appear to be most effective with good tolerability.
- Other:
 - Preclinical data suggests strains containing *linalool* may be of best benefit for anxiety.

EXPERT REPORT

4731-32-05 (C)(5) [Consideration of whether conventional medical therapies are insufficient to treat or alleviate the disease or condition]

Impact and Scope

Anxiety disorders are one of the most prevalent mental health conditions with a prevalence of up to 13.3% of people in the U.S. and have a lifetime prevalence of 28% of individuals¹. Anxiety disorders are reported to negatively impact work productivity, health, and substance use risk². There are many factors that contribute to the development of anxiety disorders: environmental stressors, medical illness, and neurologic functioning. Current treatment recommendations include starting with either counseling/therapy or medications and proceeding to a combination of both counseling/therapy and medications if initial response was inadequate³.

Efficacy of Conventional Therapies

Conventional medical therapies for anxiety disorders include Selective Serotonin Reuptake Inhibitors (SSRIs), Selective Norepinephrine Reuptake Inhibitors (SNRIs), and Benzodiazepines, just to name a few⁴. Clinical studies report that 40-50% of people with anxiety do *not* respond to conventional medical therapies⁷.

Risks of Conventional Therapies

Despite their widespread use, benzodiazepines are no longer considered first-line treatment due to risk of abuse, dependence, potential for fatal withdrawal, potential for fatal overdose, severe fall risk in elderly, and impaired cognition and coordination⁵. Unfortunately, SSRIs and SNRIs are also associated with an elevated risk of suicide⁶.

4731-32-05 (C)(6) [Evidence supporting the use of medical marijuana to treat or alleviate the disease or condition, including journal articles, peer-reviewed studies, and other types of medical or scientific documentation]

Preclinical studies using animal models of anxiety or healthy human volunteers report an anxiolytic response with certain cannabinoids⁸. (REF). Brain imaging in multiple preclinical studies consistently demonstrate that cannabidiol (CBD) is effective in reducing anxiety-related behaviors across multiple anxiety disorders with improved function in areas of the brain related to anxiety: the limbic and paralimbic system^{9, 10}. Neuroimaging studies also report that CBD attenuates human brain activity by mediating serotonin receptor transmission, reducing sensitivity of CB1 receptors, and changes in regional blood flow^{11, 12, 13, 14}.

Efficacy, Safety, & Tolerability

Clinical data reports that unlike d9-tetrahydrocannabinol (THC), cannabidiol (CBD) does not produce psychotropic or euphoric effects. Furthermore, even high-dose CBD demonstrated low abuse potential in highly sensitive populations of polydrug abusers. The effect of high-dose CBD does not approach the clinical effects of Xanax (alprazolam) or Marinol (dronabinol)¹⁵. Additionally, CBD appears to be effective in reducing THC-related anxiety side effects^{16, 17}. Like other cannabinoids, CBD appears to have a biphasic response; CBD at a low-to-moderate doses appear to improve anxiety, but at higher doses may have limited benefit^{8,10}.

The therapeutic effects of cannabis for anxiety disorders are not only limited to CBD, as preclinical and clinical data suggests that other cannabinoid and non-cannabinoid compounds found in cannabis may offer therapeutic benefit^{18, 19, 20, 21, 22}. When exposed to environmental stressors, study participants who do not use cannabis reported a subjective increase in stress reactivity and had increased blood serum concentrations of the stress hormone cortisol, however cannabis users reported decreased reactivity to environmental stressors and had no increase in blood concentrations of cortisol²³. Clinical data from a study of 42 healthy volunteers suggests that THC improved anxiety symptoms at low doses²⁴. Data from a large survey of nearly 2,830 cannabis patients reported significant reductions in anxiety and associated symptoms of irritability, insomnia, mood swings, decreased stress, muscle pain, and fatigue²⁵. Another large survey measuring 11,953 sessions of cannabis use reports that 58% of users experienced a reduction of anxiety and stress with 2 puffs of cannabis²⁶. A review of cannabis for medical use identified 8 cross-sectional studies reporting reduction of anxiety symptoms²⁷. Finally, national survey results report that patient utilization of medical cannabis has resulted in a 30% reduction in benzodiazepine prescriptions²⁸ with direct substitution of benzodiazepines for cannabis in 13% of cases²⁹.

In clinical studies, two double-blind placebo-controlled trials of CBD in children report that CBD was overall well tolerated with most adverse events being mild to moderate in severity. However, high dose CBD increases the risk of elevated liver transaminases when combined with the anti-epileptic drug valproate^{30, 31}. Fortunately, there was no drug-induced liver injury identified and liver enzymes normalized once the CBD dose or valproate dose was reduced or stopped^{32, 33}. Another double-blind placebo-controlled trial reports that, unlike prescription SSRIs and SNRIs, there is no identified suicide risk with CBD even in patients with severe psychiatric illness and rates of adverse events were similar to placebo³⁴. Currently, an active randomized, double-blind, placebo-controlled study is exploring the potential benefit of CBD for treatment of anxiety symptoms in adults who had previously had limited benefit to therapy alone³⁵.

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