

# Oregon Medical Marijuana Act Debilitating Medical Conditions Advisory Panel

## Anxiety with Depression Research Review

**NOTE:** This review considers one petition relating to depression as stated above. This petition appears to also have anxiety as underlying symptom. Research relating to cannabis dependence issues has been included only if it represents significant new information which has not been covered within the Psychotic Disorders Research Review. Depressive issues may more properly fall into the category of Mood Disorders, i.e. bipolar disorder but will be considered here to maintain consistency. Anxiety and agitation including PTSD will be considered in a subsequent review.

### 1. CONSIDERATION OF EVIDENCE

#### Description of Evidence Considered:

1. **Cannabis Indica in 19th-Century Psychiatry [Carlson, American Journal of Psychiatry, 131: 9, 1974, pp. 1004-1007.]**

A study of the history and usage of cannabis indica. The article makes frequent reports that indicate cannabis was widely prescribed by physicians in Europe and America for depressive and anxious symptoms. The...” review of the drug’s physiological and psychological effects reveals that most of the effects reported in the 1960’s were known to writers of the 19th century, when the drug was alternately considered a cure for and a cause of insanity.” “Frequently cited as a sedative, a hypnotic, or a soporific, cannabis was widely prescribed for insomnia.” “With the widespread reports of the pleasant and cheerful stimulating effects of the drug and its reduction of horrible feelings and fears, it was inevitable that cannabis was to be subjected to extensive trial in the treatment of melancholia.”

**GRADE:** Good historical evidence that cannabis was widely appreciated as an antidepressant and anxiolytic in the 19th century, prior to the pharmaceutical era.

2. **[Delta-9] Tetrahydrocannabinol in Depressed Patients [Kotin, et. al., Archives of General Psychiatry, Vol. 28: 1973, pp. 345-348.]**

Double-blind clinical trial of THC in 8 patients suffering from depression over a period of 7 days failed to produce significant euphoria or anti-depressant effect. 2 patients experienced severe anxiety reactions.

**GRADE:** Good evidence that THC does not produce an anti-depressant effect.

3. **Haschish in Melancholia [Polli, Medical Times, Vol. 100, No. 7, 1972, pp. 236-238.]**

A single case study in the 1860's of a physician using a cannabis preparation to successfully treat a woman with severe, incapacitating depression with what appeared to be psychotic features. According to the author the treatment lasted 10 days with steadily increasing doses. The cure was permanent.

**GRADE:** Fair evidence of a single case-report of incapacitating depression being successfully treated with cannabis.

**4. The Management of Treatment Resistance in Depressed Patients with Substance Use Disorders [ Nunes, et. al., The Psychiatric Clinics of North America, Vol. 19, No. 2: 1996, pp. 311-327.]**

Discusses depression and comorbid substance use with evaluation of depression and comorbid substance use and treatment recommendations. Case studies are described. It recommends a "harm reduction" approach and emphasizes the debilitating effects of ETOH and cocaine. One reference to cannabis as being perceived by patients as being harmless

**GRADE:** Good evidence that cannabis is not a significant etiological factor in depressed patients who self-medicate to relieve symptoms.

**5. The Management of Treatment-Resistant Depression in Disorders on the Interface of Psychiatry and Medicine [ Gruber, et. al., The Psychiatric Clinics of North America, Vol. 19, No. 2:1996, pp. 351-368.]**

No mention of Cannabis, no relevance to inquiry.

**GRADE:** No relevance to inquiry

**6. Advertisement for cannabis U.S.P. (American Cannabis) fluid extract Parke, Davis & Company 1929-1930 physicians' catalog of the pharmaceutical and biological products pp. 82.]**

This is an advertisement for a cannabis-based fluid extract of 80% alcohol which was distributed to physicians. "Extensive pharmacological and clinical tests have shown that its medicinal action cannot be distinguished from that of the fluid made from imported East Indian cannabis." "Narcotic, analgesic, sedative."

**GRADE:** Excellent evidence that cannabis preparations were produced and advertised to physicians and were indicated as a sedative.

**7. Do patients use marijuana as an antidepressant? [Gruber et.al., Depression 4(2): 1996, pp. 77-80.]**

The authors "present 5 cases in which the evidence seems particularly clear that marijuana produced a direct antidepressant effect. If true, these observations argue that many patients may use marijuana to "self-treat" depressive symptoms."

**GRADE:** Good case study evidence that some patients use cannabis to treat depressive symptoms.

## **7. Petitioner application and information submitted with application**

The petitioner and her husband submitted documents including a letter to the State Health Officer describing her diagnosis by two doctors of “Clinical Depression and High Anxiety.” She also testified by telephone at the March 20th meeting.

Petitioner states:

“The depression/anxiety is nothing new for me as I have struggled with this for most [of] my life with relief only from smoked Marijuana.”

She repeatedly emphasizes less than acceptable results from medications. Her petition is attached to 11 pages of chart notes from her physician, which indicates a gradual decrease of functioning over the 2-3 years of treatment. Chart notes indicate treatment with Paxil, Buspar, Prozac, Lithium, Xanax, Luvox, and Thorazine. The notes indicate some psychotic symptoms of varying frequency and duration as well as fluctuating weight. The doctors’ notes state:

“ I feel that the patient may benefit from medical marijuana to help control her anxiety, but I told her that I would not prescribe this because it does not fall within the guidelines for treatment with medical marijuana.”

The petitioner appears also to be prescribed long-term benzodiazepines. Petitioner states:

“Marijuana eliminates the need for Xanax. It does not produce withdrawal as with Xanax. I can smoke Marijuana without a problem.”

The petitioner relays by telephone that she doesn't get “high” and smokes every few hours. Her partner states that legal drugs haven't helped. “Legal drugs make her dysfunctional.” “Marijuana seems to work for her.”

**GRADE:** Good evidence that this severely incapacitated individual benefits from using cannabis and that cannabis is a drug of last resort after trials of many drugs have failed and she has been on long-term benzodiazepines.

### **Clinical Effectiveness (and comparison with established alternatives)**

This research base describes significant although slim empirical evidence of cannabis’ usefulness for depression. There is good evidence that cannabis falls well within established safety parameters especially when compared with commonly used anti-depressant and mood-stabilizing drugs. Clinical trials are scant and tend to indicate minimal if any anti-depressant effect.

### **Health Benefits and Risks:**

Health benefits appear to be related to increased medication toleration by minimizing side effects, and possibly exerting some anti-anxiety effect, which lifts

the cloud of despondency, and hopelessness, which is common with, depressed persons. Risks include the potential for dependence associated with long-term heavy use and the possibility that cannabis may mask or cover symptoms depressive symptoms rather than actually relieve them.

### **Factors Affecting Safety, Effectiveness, and Related Considerations for All Patients and for Specific Patient Types.**

Safety factors appear to favor cannabis. There is no clear evidence that cannabis use exacerbates suicidal ideation in depressed patients without psychotic symptoms. Factors related to effectiveness are not clear other than underlying substance dependence or perhaps liver disease, which may alter cannabinoid metabolism or interact with other medications.

What is clearer is that depression carries with it high mortality rates due to suicide. Additionally, depression interferes with energy and enjoyment. Factors, which affect safety, include the side effects of commonly used medications. These side effects may cause significant harm or death, as with MAOIs. The relative harm associated with cannabis appears minimal when compared with side-effect profiles of many drugs used to treat depression-most notably Lithium. Cannabis appears effective in a small but unknown percentage of depressed persons who do not suffer from underlying substance use disorders.

### **Net Health and Overall Impact of Medical Marijuana Use for This Condition:**

Please see above

### **Other Considerations**

As is the case with all psychiatric conditions evaluated, the legal status of cannabis remains the single biggest detriment to ill persons through contact with law-enforcement or illegal drug networks. Depressed patients sometimes act in a suicidal manner in response to hopelessness and despair. The trauma of arrest and prosecution may be considered a potential risk factor for suicide.

## **II. Performance On Assessment Criteria**

**1. Quality and Sufficiency of Available Evidence:** *There is sufficient available evidence of sufficient quality to permit reaching a sound determination relating to the use of medical marijuana for the treatment of this condition.*

**NO**

**Comments:** Few if any carefully controlled clinical trials have been done to measure cannabis' antidepressant effect. The case histories and "N of 1" studies which have been done indicate that cannabis' anxiolytic properties may actually represent the underlying mechanism of it's anti-depressant effect, rather than a primary anti- depressant effect.

2. [A] Clinical Effectiveness: *The use of medical marijuana for this condition is clinically effective.*

**POSSIBLY**

**Comments:** For some percentage of patients suffering from depression cannabis is effective.

[B] **Relative Clinical Effectiveness:** *The use of medical marijuana for this condition is clinically effective relative to established alternative treatments for this condition.*

**NAD**

**Comments:** Insufficient data is available to evaluate relative clinical effectiveness due to a lack of randomized clinical comparison trials with commonly used antidepressants.

3. **Health Benefit/ Risk Ratio:** *The health benefits of medical marijuana use for this condition outweigh the health risks.*

**POSSIBLY**

**Comments:** For those who do not suffer from comorbid substance use disorders, and have exhausted their medical alternatives the benefits of cannabis use under medical supervision outweigh the risks-especially when compared with the statistical likelihood of suicide.

4. **Net Health Impact:** *The use of medical marijuana for this condition improves net health outcomes (functional status and/or ability to perform activities of daily living) for those individuals with this condition who use medical marijuana.*

**NAD**

**Comment:** The extent to which cannabis use creates a net health impact is unknown at this time.

5. **Net Overall Impact:** *The use of medical marijuana for this condition improves net overall outcomes (quality of life and/or perceived satisfaction with condition improvement) for those individuals with this condition who use medical marijuana.*

**NAD**

**Comments:** Net overall impact is difficult to assess until randomized clinical trials have been conducted. For the petitioner, at least, there appears to be a net overall benefit in her quality of life as perceived by her, her physician, and partner.

**6. Safety, Effectiveness, or Related Issues:** *There are no such compelling or overriding issues that alter any of the determinations regarding the use of medical marijuana for the treatment of this condition that would have been reached absent these issues.*

**YES**

**Comments:** The potential danger to the petitioner as well as other depressed patients who use cannabis by contact with the legal system cannot be overstated. These potentially violent confrontations with police and/or illegal drug networks may result in death directly, or through suicide.

### **III. Overall Findings and Recommendations**

Summary of Findings:

One (1) petitioner's written and oral comments appear to support therapeutic use of cannabis for depression;

Two (2) surveys detailing the history of cannabis for treating depression and treatment guidelines for depressed people;

One (1) pharmaceutical advertisement indicating that cannabis was prescribed by physicians for insomnia in this century;

One (1) clinical trial indicating no anti-depressant effect from THC in clinical surroundings.

One (1) clinical trial indicating efficacy of THC in treating insomnia;

One (1) survey of no relevance.

**Recommendation Regarding Adding this Condition to the list of "Debilitating Medical Conditions" for Purposes of the Oregon Medical Marijuana Act**

**Add disease to list of disease conditions pursuant to ORS 475.302(2)(a)**

**COMMENTS:** This "yes" recommendation is based upon the following rationale: It is medically indefensible and contrary to the ethics of the nursing profession for me to advocate that ill people be arrested and jailed for their use of cannabis. This situation has arisen because of Federal abdication of research protocols, which would have long-since clarified cannabis' relative value. Ill Oregonians should not bear the weight of this governmental negligence. Furthermore, the taxpayers of Oregon should not be saddled with the costs of processing ill people through the criminal justice system. This represents an unfair burden to patients and taxpayers and will further alienate depressed people from accessing the medical system.

I would make the following recommendations for depressed patients and their doctors wishing to avail themselves of cannabis, should depression be approved for inclusion on the list of debilitating medical conditions:

1. The patient should be refractory to more efficacious treatments like SSRIs,

2. The patient should have no history of significant dependence issues with alcohol, tobacco, or psychoactive drugs.
3. The patient should be, and remain under the care of a physician or nurse practitioner.
4. The patient should have periodic assessments to determine the presence or severity of suicidal ideation.
5. The patient should be willing to trial new anti-depressants providing they have the financial means to do it.
6. The patient should be educated about the potential side effects of cannabis including cognitive, pulmonary, and dysphoric.

**RATIONALE Re: this recommendation**

The rationale for this decision is related to the unavoidable political climate in which elected leaders support laws which are in direct opposition to the safety and benefit of ill Oregonians. This was clearly articulated by Oregon voters in November of 1998 by the simultaneous passage of the Oregon Medical Marijuana Act, while at the same time rejecting an increase in criminal penalties for all cannabis use. The sentiments of Oregonians appear to favor removing ill Oregonians from the criminal justice system. Thus, in spite of the meager amount of evidence demonstrating efficacy for the treatment of depression with cannabis, I recommend including it within the protections of the OMMA. Since depression may also be thought of as a symptom as well as a disease entity, the inclusion of the symptom of “severe depression” may fulfill patient need adequately and allow this decision to be made in a physician’s office instead of a District Attorney’s office.

***Submitted by:***

***Edward Glick, RN***

***Date: March 27, 2000***