

# Oregon Medical Marijuana Act Debilitating Medical Conditions Advisory Panel

## Anxiety Disorders: Post Traumatic Stress Disorder, Insomnia with Anxiety, and Agitation/Anxiety Associated with Alzheimer's Disease –

### Research Review

**NOTE:** This review considers four petitions relating to anxiety as stated above. These conditions appear to have anxiety and agitation as underlying symptoms. 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. Due to symptom overlap between depression and anxiety some research will appear in both reviews.

#### 1. CONSIDERATION OF EVIDENCE

##### Description of Evidence Considered:

###### 1. Petitioner #1, petition and live interview

The applicant is the wife of a man suffering from Alzheimer's dementia with an underlying anxiety state. She relays that cannabis:

“has helped my husband to reduce the constant pacing and his uncooperativeness in the form of agitation. He is able to sit quietly without any anxiety after having marijuana.”

The patient's physician has submitted the following note written in the comment section of an application to the OMMA:

“Pt has Alzheimer's Disease and associated agitation- MMJ relaxes him and controls agitation.”

**GRADE:** Good self-report that cannabis smoking helps sedate the patient and results in decreased anxiety.

###### Petitioner #2, petition and live interview.

This petitioner is a woman suffering from posttraumatic Stress Disorder (PTSD) as a result of multiple traumas that were not explored. She submits two letters and a bibliography describing her vocational background. She says that she presently has a “card” to use medical cannabis. (For chronic pain due to fibromyalgia.) She writes: “ I am able to get out of bed, go to my volunteer job....” There are few descriptions of her actual use patterns, but she did describe the

lowering of fears and anxieties she obtains from her use of cannabis. She feels that it is a spiritual healing tool that helps her deal with the traumas of the past, and says her frequency and dosage have not changed. She can tell the difference between different varieties in how effective they are at controlling her symptoms. The bibliography attached lists 43 references which were submitted with her application but have not been included with the evidence base. Many of these references appear to have limited relevance.

**GRADE:** Fair evidence that this patient is benefiting from her use of cannabis but her presentation is so complex that it is difficult to assess overall health benefit versus risk.

### **3. Petitioner #3- petition and live interview.**

This petitioner relays that cannabis helps his insomnia. “It also seems to decrease the number of nightmares about Nam and killing.” He describes the process of anxiety attacks developing as “butterflies in my stomach.” This develops to nausea, insomnia, nightmares, and dry heaves.

“If I can smoke some marijuana in the early stages of the anxiety attack it doesn’t progress to the painful cramps and spasms and calms and relieves my nausea.”

The petitioner’s physician has written the following, which is included in his petition:

“ Mr. \_\_\_ suffers from post traumatic stress syndrome. He has been tried on a variety of antidepressants. The only medicine that he feels able to function on is cannabis and I would recommend he continue with this drug.”

Two studies are attached to the petitioner’s application that will be included below.

**GRADE:** Good, though slim evidence that this patient is benefiting from his use of cannabis under the guidance and agreement of his physician.

### **4. Petitioner #4- petition and live interview.**

Petitioner #4 is a 46-year-old white male who uses cannabis on an occasional basis to help him go to sleep. 10 pages of progress notes are attached which indicate that he suffers from chronic anxiety and insomnia. He has repeatedly discussed his use of cannabis to help him sleep as well as assist him with Benzodiazepine withdrawal symptoms with his physician. (He has been taking Valium for ten years per physician notes.) Six pages of information concerning the symptoms and course of “Benzodiazepine Withdrawal Syndrome” are attached to petition. Petitioner smokes tobacco, denies ETOH use.

**GRADE:** Fair to good evidence that the petitioner benefits from his use of cannabis through its anxiolytic effect.

**5. Ranking of risks of 6 commonly used drugs by Dr. Jack Henningfield (NIDA)...and Dr. Neal Benowitz (UCSF) [New York Times, August 1994, C3.]**

In rankings of Nicotine, Heroin, Cocaine, Caffeine, and cannabis, cannabis is rated least serious in withdrawal symptoms, least serious in reinforcement, least serious in tolerance, least serious in dependence, and moderately intoxicating (alcohol rated most serious.)

**GRADE:** Excellent evidence that cannabis is low on the abuse and dependence continuum of psychoactive drugs.

**6. Factors relating to current marijuana use by Vietnam War veterans in recovery from addiction to other drugs or chemicals of abuse [ Newton, et. al., Department of Veterans Affairs Research and development Information System (RCS 10-0159).]**

This research consisted of an anonymous questionnaire given to veterans treated in the Stratton VA Medical Center. It was based upon staff observations that Vietnam combat veterans discontinued their use of alcohol and illicit drugs except cannabis. Results indicated that the PTSD group more often used cannabis to:

1. Help with sleep;
2. Decrease nightmares;
3. Prevent bad thoughts of the past;
4. And improve self-esteem.

The authors conclude that “data support the contention that marijuana can be used for ‘self medication’ of psychiatric problems.”

**GRADE:** Good survey evidence that cannabis may benefit Vietnam veterans suffering from PTSD related experiences.

**7. Personal correspondence from Dr. Tod Mikuriya.**

Dr. Mikuriya states: The persons who suffer from PTSD in my practice who medicate with cannabis have discovered that the drug is by far the most effective in controlling the symptoms of anxiety attacks and insomnia.

**GRADE:** Good survey evidence that Dr. Mikuriya has encountered many patients who effectively treat their symptoms with cannabis.

**8. Cannabis Use and Cognitive Decline in Persons under 65 Years of Age [ Lyketsos, et. al., American Journal of Epidemiology, Vol. 149, No. 9: 1999, pp. 794-800.]**

This study analyzed 1,318 persons over time (12) years through the Mini-Mental State Exam. It concluded: “There were no significant differences in cognitive decline between heavy users, light users, and non-users of cannabis.”

**GRADE:** Good epidemiological evidence that users of cannabis do not suffer from cognitive decline, although of limited relevance.

**9. Specific attentional dysfunction in adults following early start of cannabis use [Ehrenreich, et. al., Psychopharmacology 142: 1999 pp. 295-301.]**

The objective of the study was to test whether cannabis use among preteens caused brain alterations in humans, or interfered with development. The results of the study indicate that “Early-onset users [before age 16] showed significant impairments in reaction times” suggesting that cannabis use during adolescence may lead to enduring effects.

**GRADE:** Good evidence that early-onset cannabis use may negatively affect human maturation processes. Minimal relevance to this inquiry.

**10. Acute administration of the CB-1 cannabinoid receptor antagonist SR 141716A induces anxiety-like responses in the rat. [Navarro, et. al., NeuroReport 8: 1997, pp. 491-496.]**

Rats were administered SR 141716A, a cannabinoid antagonist. The results indicate that : “ the CB-1 receptor antagonist SR 141716A elicited defensive responses in rats in two behavioral models of anxiety, suggesting the existence of an endogenous cannabinoid tone involved in regulation of the emotional responses.”

**GRADE:** This represents good animal research indicating that the endogenous cannabinoids system in mammals is a factor in regulating emotional response. This may lend credence to a hypothesis that cannabis (which binds with endogenous CB-1 and CB-2 receptors in mammals), may exert anxiolytic effects.

**11. Action of Cannabidiol on the Anxiety and other Effects Produced by [delta-9] THC in Normal Subjects [ Zuardi, et. al., Psychopharmacology 76: 1982, pp. 245-250.]**

The objective of this research was to determine whether CBD exerts an anti-anxiety effect in persons treated with THC, in 8 volunteers. The author’s state: “ It was verified that CBD blocks the anxiety provoked by THC, however this effect was also extended to other marijuana-like effects and to other subjective alterations.”

**GRADE:** Good experimental evidence that CBD attenuates the anxiety-producing effects of THC alone and that cannabis may decrease anxiety.

**12. Chronic PTSD in Vietnam Combat Veterans: Course of Illness and Substance Abuse [ Bremner, et. al., AM journal of Psychiatry 153:3: 1996, pp. 369-375.]**

This study was aimed at assessing the role and significance of Alcohol and psychoactive drugs in the presentation of PTSD symptoms, as well as describe

patterns of morbidity over time. 61 Vietnam combat veterans were interviewed with various PTSD rating assessments. Results indicate that symptoms of PTSD begin soon after exposure to trauma...“that the natural course of alcohol and substance abuse parallels that of PTSD.”

**GRADE:** Fair value of an association between cannabis use and PTSD but cannabis not independently studied separate from alcohol. Of questionable value except that it clearly establishes a link between cannabis and PTSD.

13. **Generalized Anxiety Disorder Longitudinal Course and Pharmacologic Treatment [Schweitzer, The Psychiatric Clinics of North America, Vol. 18, No. 4: 1995, pp. 843-845.]**

[No mention of cannabis, no relevance to inquiry]

14. **Pharmacotherapy for Post-Traumatic Stress disorder [Sutherland, et. al., Psychiatric Clinics of North America Vol. 17, No. 2: 1994, pp. 409-423.]**

[No relevance to cannabis; no relevance to inquiry]

15. **Anxiety in the Elderly [Sheikh, et. al., The Psychiatric Clinics of North America Vol. 18, No. 4: 1995, pp. 871-883.]**

[No reference to cannabis; no relevance to inquiry]

16. **Insomnia and Related Sleep Disorders [Mendelson, The Psychiatric Clinics of North America Vol. 16, No. 4:1993, pp. 841-851.]**

This article describes “psychophysiologic insomnia” as refractory to conventional treatments and the different treatments which are used. There is no reference to cannabis.

**GRADE:** No relevance to inquiry.

17. **Post traumatic stress disorder among substance users from the general population [Cottler, et.al., American Journal of Psychiatry 149(5): 1992, pp. 664-70.]**

This report comprised of a one-page research abstract, which used epidemiological catchment data to “evaluate the prevalence of PTSD in substance users in the general population.” The results indicated that: “cocaine/opiate users are over three times as likely as comparison subjects to report a traumatic event.” No mention is made of cannabis.

**GRADE:** Questionable relevance to this inquiry except that cannabis is not linked statistically with PTSD, unlike cocaine and opiates.

18. **Medical Marijuana and posttraumatic Stress Disorder [No author listed, no publication listed, missing pages 2 and 3.]**

This report comprises part history of PTSD and part testimonial. The history section makes no mention of cannabis. The testimonial page describes a wife of

a veteran emphasizing that if her husband smokes marijuana before the “rage gets to the point of no return,” he becomes “visibly calmer and more relaxed.”

**GRADE:** Fair evidence of a single case report of efficacy for controlling PTSD symptoms.

19. **Marijuana and Medicine: Assessing the Science Base; Institute of Medicine, 1999, pp. 5.]**

Executive summary conclusion: “ The psychological effects of cannabinoids, such as anxiety reduction, sedation and euphoria can influence their potential therapeutic value. Those effects are potentially undesirable for certain patients and situations and beneficial for others.”

**GRADE:** Convincing survey evidence that cannabis is used to decrease anxiety in some patients suffering from anxiety disorders.

20. **The Ressonant Brain [Conrad, Hemp for Health: pp. 74.]**

A one-page description of the Federal research program described in #6 above

Redundant article cited elsewhere.

21. **Cannabisprodukten im deutschen Sprachraum {The use of cannabis products in Germany} [Forsch Komplementarmed Suppl. S3: 1999, pp. 28-36.]**

170 subjects participated in an anonymous standardized survey. Questionnaires of 128 respondents were included. Most frequent mentioned indications for using cannabis were the following:

Depression (12%),  
Sleeping disorders (4.8%),

**GRADE:** Good, though slim survey evidence that Europeans use cannabis to reduce anxiety, assist with sleep and decrease depression.

22. **Summary of 2,480 medical marijuana patients interviewed by Dr. Tod Mikuriya [Submission to the Association for Cannabis Medicine.]**

This paper summarizes ICD classifications for diseases and categorizes the data according to mentions of cannabis use. The results indicate that: “2.9% of Dr. Mikuriya’s medical cannabis patients have a primary diagnosis of insomnia.” According to the table, 26% of his patients comprising 660 patients use cannabis for mood disorders including depression, anxiety disorder, attention deficit disorder, and panic disorder.

**GRADE:** This is excellent and extensive case-report evidence that cannabis is used by many persons to treat agitation, insomnia and depression.

**23. Therapeutic Application of Marijuana [Walton- Article taken off Internet , Unspecified source.]**

This article summarizes historical uses of cannabis by breaking indications down into categories. One such category is: “Sedative and Hypnotic Action.” This section quotes an “early experimenter” as saying: “ in its hypnotic and soothing effects on the nervous system, its resemblance to morphia is great.”

**GRADE:** Fair historical evidence that cannabis was used for its sedative and anti- anxiety effects by physicians in the 19th century.

**24. A Survey of 100 Medical Marijuana Club Members [ Harris, et. al., Drug Dependence Research Center, UCSF, no date,]**

100 cannabis club members were surveyed as to their reasons for using cannabis. Users: “perceived marijuana to be more effective with less severe side-effects than other treatments.” A history of substance abuse or dependence was present in 87% and of other psychiatric disorders in 83%.

**GRADE:** Good, though slim evidence that a large percentage of medical cannabis users suffer from either drug-dependence or comorbid psychiatric issues.

**25. The Healing Herbs, [The Rodale Herb Book, no author, publisher listed ,pp. 94-95.]**

Under the section titled “sedatives” is a brief discussion of cannabis which states: “...marijuana may well ‘find application in the treatment of certain forms of psychiatric illness’ such as depression.”

**GRADE:** Poor evidence of psychiatric usefulness, with no evidence base referred to other than that it “has a centuries-old history of use for sedative and religious purposes.”

**26. Cannabis Indications Article. [No citation.]**

This article describes various indications for cannabis, among them “Psychological Effects- Stress reduction” The article states that stress-reduction: “...is a nearly universal benefit of cannabis use.”

**GRADE:** Fair though limited reference to cannabis as an anxiolytic.

**27. 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.]**

It describes a fluid extract of cannabis resins and 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.

**28. Marijuana Use and Mortality [Sidney, et. al., American journal of Public health, Vol. 87, No. 4: 1997, pp. 585-590.]**

This study included over 65,000 people who completed a questionnaire about smoking habits that included cannabis use from 1979-1985. A mortality analysis was conducted in 1991. Results indicate that: "...current marijuana use was not associated with a significantly increased risk of [non-AIDS] mortality."

**GRADE:** Excellent evidence that cannabis use in general does not cause an increase in mortality, however questionable relevance to it's application in psychiatric populations, and to this inquiry.

**29. Insomnia-Personal Comments [Oerther: 1999.]**

This self-report describes the use of cannabis by a physician practicing medicine in an Evacuation Hospital in Vietnam in 1969. The author reports that cannabis assisted him with sleep. " I enjoyed six or eight inhalations from a burning dispenser and followed with the first quiet dreamless, nightmareless solid uninterrupted eight hours of sleep in months. I had to get through another 2 suckass months of war, but as long as I was able to get my inhalations, I could sleep through the night."

**GRADE:** Good evidence of a person working in Vietnam during the war who used cannabis to assist with sleep as well as decrease nightmares.

**30. Anxiety-Personal Comments [unknown author, 2000.]**

This is a hand-written one-page letter from a person suffering from Lupus, fibromyalgia, anxiety, bipolar disorder, and degenerative arthritis. This person reports that: "I take 17-18 pills a day just to maintain a modicum of health." "I speak only for myself when I say that using marijuana dulls the pain, allows me to be creative, feel ambitious, less stressed and allows me to sleep."

**GRADE:** Good evidence of personal comments that report several medical indications for cannabis use.

**31. [Delta-9] THC an an Hypnotic: An Experimental Study at Three Dose Levels [ Cousens, et. al., Psychopharmacologia (Berl.) 33: 1973, pp. 355-364.]**

THC was found to significantly decrease the time it took healthy insomniacs to fall asleep. Three dosage levels were tried with nine subjects tested once a week for six weeks. The most effective dose was the 20-mg. level.

**GRADE:** Good experimental evidence that cannabis has sedative properties.

**32. 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 and cited 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 evidence that cannabis was widely appreciated as an antidepressant and anxiolytic in the 19th century, prior to the pharmaceutical era.

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

There is significant historical and personal reference to the effectiveness of cannabis for agitation and/or anxiety within this evidence base, comprised mostly of self-reports and surveys.

**Health Benefits and risks:**

Health benefits appear to be related to the promotion of sleep as a stabilizing factor in user’s overall functioning.

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

There are several issues relating to the petitioners and others with anxiety and/or sleep disturbance who use cannabis.

1. **Legal status:** The criminal penalties and associated contacts with police include arrest, search and seizure of assets conviction and potentially incarceration for the petitioners. Also, contacting the illegal cannabis market carries with it attendant risks which include ingestion of adulterated cannabis and contact with potentially violent black market people.

2. **Cannabis dependence:** The potential for cannabis dependence exists primarily in chronic heavy users of cannabis. Those who use cannabis to assist in sleep or decrease anxiety should be aware of the signs, which indicate severe dependence. The overall likelihood that cannabis dependence is a major contraindication for anxiety is minimal, (as opposed to schizophrenia.)

**3. Respiratory complications:** Long-term heavy cannabis smoking is associated with an increase of risk for pulmonary complications which some studies report exceeds that of tobacco use. The petitioners should attempt to minimize these risks by consuming high-potency cannabis in smaller amounts and considering alternative dosing arrangements such as vaporizers or eating.

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

The net health impact and overall impact for the petitioners is that long-term cannabis use is benefiting them to varying degrees. There clearly is strong evidence, based upon many self-reports and historical descriptions that the overall impact of cannabis use for those suffering from PTSD-like symptoms is beneficial.

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

Cannabis use among persons suffering from anxiety-like symptoms appears to be indicated for some significant but unknown percentage of those who use it. No case-controlled studies comparing its efficacy in comparison to standard treatments have been done to my knowledge; therefore this conclusion is based upon self-reports and case histories. In the case of Alzheimer's dementia and agitation there is clear evidence that the patient is benefiting relative to his prognosis and medical alternatives but it is impossible to extrapolate to what degree this treatment may benefit others in similar circumstances.

**Other Considerations**

**NO**

**Comments:** There is an absence of clinical trials differentiating and exploring the research base which would describe on a neurochemical level why cannabis exerts anxiolytic effects, only that it does.

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

**POSSIBLY**

**Comments:** Cannabis is clinically effective for some significant percentage of persons suffering from symptoms of anxiety/ insomnia. This percentage is probably greater than that for schizophrenic disorders.

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

**YES**

**Comments:** Behavioral therapies in conjunction with hypnotic drugs appear to be the standard therapies used to combat insomnia and agitation. Cannabis is at

least as effective as benzodiazapines with lower overall toxicity for patients who either are refractory to those treatments or cannot afford them.

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

**POSSIBLY**

**Comments:** There is convincing historical and subjective evidence that cannabis use creates a net health benefit for those persons who are not at high risk for significant dependence or pulmonary risk.

**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.*

**YES**

**Comments:** For the petitioners as a whole the net health benefit is clear. For the petitioner who is representing her husband with degenerating Alzheimer's Disease the benefit is clear.

**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.*

**POSSIBLY**

**Comments:** This question will only be satisfactorily answered by clinical trials.

**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 issue of the legal status of chronically ill people alters these determinations in the following way: The United States Government policy of hindering research into the potential therapeutic uses of cannabinoids creates a "catch-22" for patients who use the drug. Research is routinely obstructed through a long and cumbersome process. Those opposed to access to cannabis then use this lack of research as a justification to continue the present policy of criminalizing ill people who use the drug. To date only one study protocol exploring cannabis' medical utility is ongoing a full year after the Institute of Medicine's Report calling for more research. A research protocol by Dr. Abrams of UCSF was only allowed to proceed after the focus was changed to a search for the drug interactions of cannabinoids and protease inhibitors, instead of a comparison of efficacy. This continuing Federal policy of obstruction has created

a situation where high-grade evidence of clear medical utility is nearly impossible to obtain or corroborate. Until this research is allowed to proceed it is indefensible on a humanitarian grounds to forbid access to cannabis for patients who are under a physician's care and who suffer severe symptoms. The patient should be the person to decide if cannabis is justified as a medical treatment in consultation with the physician. These determinations may be altered in the future by development of new therapeutic cannabinoid delivery vehicles, and by a governmental policy which does not cause more apparent harm to ill people than their use of cannabis.

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

#### Summary of Findings

This review included the following:

Four (4) petitioner's written and oral testimony including Alzheimer's dementia, Agitation, Insomnia, and 2 petitions for PTSD;  
Five (5) written personal comments describing what the authors' consider effective use to control agitation, insomnia and/or PTSD;  
One (1) Pharmaceutical advertisement out of a 1930 catalog of pharmaceuticals advertising cannabis tincture for insomnia;  
Five (5) articles describing cannabis' history of use;  
Five- (5) research studies describing various cognitive, mortality statistics, receptor interaction effects, and questionnaires of use;  
Three (3) surveys of use;  
Seven (7) journal articles describing various aspects of PTSD, anxiety and insomnia, some of which have little apparent relevance to this inquiry.

#### **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)**

The following conditions may assist in medical guidance for persons with anxiety/ Insomnia/PTSD who are participating in the OHD Marijuana Registry program:

- A. The patient should be refractory to more conventional treatments;
- B. The MD should conduct periodic reviews of use to determine presence of excessive use (i.e. increasing dosage and frequency, signs of decreasing effectiveness and decreasing function.);
- C. The MD should periodically evaluate pulmonary function for those who smoke cannabis and recommend high-potency cannabis;

D. The MD should consider “N-of-1” research evaluations to augment the research base;

E. The MD should carefully evaluate hepatic and neurochemical interactions with initiation of any new pharmacotherapy.

**COMMENTS:**

**RATIONALE Re: this recommendation**

The “default” position of the OHD should be to include severe anxiety to the list of debilitating medical conditions covered under the Oregon Medical Marijuana Act. Oregonians suffering from these persistent incapacitating disorders should not be subject to criminal prosecution for their use of cannabis. They also should not be forced to assume the costs of applying to the program. The obvious lack of “high-grade” randomized clinical comparisons is not sufficient reason to forbid access to the registry card program for patients whose behavior poses little or no risk to the State of Oregon. On the contrary, it is an unfair burden to place upon the People of Oregon to pay for the costs associated with arresting, prosecuting, and incarcerating ill people who use cannabis.

**NOTE:** Anxiety /agitation are commonly thought of as symptoms. It may be more appropriate to include “severe anxiety” as a symptom designation within the OMMA.

**Submitted By:**

**Edward Glick, RN**

**Date: March 28, 2000**

**Oregon Medical Marijuana Act  
Debilitating Medical Conditions Advisory Panel  
Disease-Specific Recommendations**

**PTSD Research Review**

**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:** There is a lack of understanding based upon randomized clinical trials of why those with PTSD seem to have such a strong affinity for cannabis-only that it is widely used to treat the intrusive thoughts and feelings.

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

**YES**

**Comments:** For a significant percentage of PTSD sufferer's cannabis is effectively used.

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

**YES**

**Comments:** PTSD is often treated with long-term benzodiazapines and sometimes by anti-depressants. It is clear that the effects of cannabis are no worse and probably much less harmful as long as there are no underlying psychotic tendencies.

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

**YES**

**Comments:** There may be a large number of Oregonians- especially combat veterans who would benefit from cannabis as long as there is adjunctive psychotherapy or some other healing process.

**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.*

**YES, POSSIBLY**

**Comments:** Cannabis use for PTSD may be helpful as long as significant substance use issues do not contribute to loss of functioning. Net health impact is moderately positive under medical supervision.

**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.*

**YES, POSSIBLY**

**Comments:** Cannabis is probably safer than other pharmaceuticals and certainly will lessen panic and traumatic thoughts in those who use it.

**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:** Please see general statement under Anxiety Disorders.

**III. Overall Findings and Recommendations**

Summary of Findings

Two petitioners submitted information for PTSD. The first is a woman with a complex medical history who endorses that it assists her in her healing processes from multiple childhood traumas. The second is a Vietnam combat veteran who uses it to treat his agitation related to: “thoughts of Nam and killing.” I would give slightly higher grade of evidence to the veteran.

Other significant evidence:

**6. Factors relating to current marijuana use by Vietnam War veterans in recovery from addiction to other drugs or chemicals of abuse [Newton, et. al., Department of Veterans Affairs Research and development Information System (RCS 10-0159).]**

This research consisted of an anonymous questionnaire given to veterans treated in the Stratton VA Medical Center. It was based upon staff observations that Vietnam combat veterans discontinued their use of alcohol and illicit drugs except cannabis. Results indicated that the PTSD group more often used cannabis to:

1. Help with sleep;
2. Decrease nightmares;
3. Prevent bad thoughts of the past;
4. And improve self-esteem.

The authors conclude that “data support the contention that marijuana can be used for ‘self medication’ of psychiatric problems.”

**GRADE:** Good survey evidence that cannabis may benefit Vietnam veterans suffering from PTSD related experiences.

**7. Personal correspondence from Dr. Tod Mikuriya.**

Dr. Mikuriya states: The persons who suffer from PTSD in my practice who medicate with cannabis have discovered that the drug is by far the most effective in controlling the symptoms of anxiety attacks and insomnia.

**GRADE:** Good survey evidence that Dr. Mikuriya has encountered many patients who effectively treat their symptoms with cannabis.

**10. Acute administration of the CB-1 cannabinoid receptor antagonist SR 141716A induces anxiety-like responses in the rat. [Navarro, et. al., NeuroReport 8: 1997, pp. 491-496.]**

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**GRADE:** This represents good animal research indicating that the endogenous cannabinoids system in mammals is a factor in regulating emotional response.

This may lend credence to a hypothesis that cannabis (which binds with endogenous CB-1 and CB-2 receptors in mammals), may exert anxiolytic effects.

**12. Chronic PTSD in Vietnam Combat Veterans: Course of Illness and Substance Abuse [Bremner, et. al., AM journal of Psychiatry 153:3: 1996, pp. 369-375.]**

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**GRADE:** Fair value of an association between cannabis use and PTSD but cannabis not independently studied separate from alcohol. Of questionable value except that it clearly establishes a link between cannabis and PTSD.

**14. Pharmacotherapy for Post-Traumatic Stress disorder [Sutherland, et. al., Psychiatric Clinics of North America Vol. 17, No. 2: 1994, pp. 409-423.]**

No direct relevance to cannabis; however, good descriptions of PTSD and pharmacological options.

**17. Post traumatic stress disorder among substance users from the general population [Cottler, et.al., American Journal of Psychiatry 149(5): 1992, pp. 664-70.]**

This report comprised of a one-page research abstract, which used epidemiological catchment data to “evaluate the prevalence of PTSD in substance users in the general population.” The results indicated that: “cocaine/opiate users are over three times as likely as comparison subjects to report a traumatic event.” No mention is made of cannabis.

**GRADE:** Questionable relevance to this inquiry except that cannabis is not linked statistically with PTSD, unlike cocaine and opiates.

**19. Marijuana and Medicine: Assessing the Science Base; Institute of Medicine, 1999, pp. 5.]**

Executive summary conclusion: “The psychological effects of cannabinoids, such as anxiety reduction, sedation and euphoria can influence their potential therapeutic value. Those effects are potentially undesirable for certain patients and situations and beneficial for others.”

**GRADE:** Convincing survey evidence that cannabis is used to decrease anxiety in some patients suffering from anxiety disorders.

**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:**

It should be noted that PTSD is often complicated by substance use disorders. I would recommend that it be approved as long as physicians monitor use and actively use cognitive and behavioral therapies to heal the wounds.

**RATIONALE Re: this recommendation**

[Please see general rationales.]

***Submitted by:***

***Edward Glick, RN***

***Date: March 28, 2000***

**Oregon Medical Marijuana Act  
Debilitating Medical Conditions Advisory Panel  
Disease-Specific Recommendations**

**INSOMNIA WITH ANXIETY Research Review**

**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.*

**YES**

**Comments:** There is a large body of historical and self-reports of efficacy. Clinical trials are mostly absent.

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

**YES**

**Comments:**

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

**YES**

**Comments:** Relative to inadequate treatments for severe insomnia and the functional decompensation which results from this disease, cannabis may be beneficial.

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

**YES**

**Comments:** Health benefits are significant related to overall ability to function. Risks appear minimal.

**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.*

**YES**

**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.*

**YES**

**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.*

[Please see general statement]

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

#### Summary of Findings

Two petitioners seem to be helped by using cannabis to treat insomnia. The first is the Vietnam veteran who says it helps him sleep. The second is the petitioner using it for Benzodiazepine withdrawal. Both cases represent moderately persuasive evidence of therapeutic use based upon a superficial understanding of medical records.

Other research of significance:

**11. Action of Cannabidiol on the Anxiety and other Effects Produced by [delta-9] THC in Normal Subjects [ Zuardi, et. al., Psychopharmacology 76: 1982, pp. 245-250.]**

The objective of this research was to determine whether CBD exerts an anti-anxiety effect in persons treated with THC, in 8 volunteers. The author's state: "It was verified that CBD blocks the anxiety provoked by THC, however this effect was also extended to other marijuana-like effects and to other subjective alterations."

**GRADE:** Good experimental evidence that CBD attenuates the anxiety-producing effects of THC alone and that cannabis may decrease anxiety.

**16. Insomnia and Related Sleep Disorders [Mendelson, The Psychiatric Clinics of North America Vol. 16, No. 4:1993, pp. 841-851.]**

This article describes” psychophysiologic insomnia” as refractory to conventional treatments and the different treatments which are used. There is no reference to cannabis.

**19. Marijuana and Medicine: Assessing the Science Base; Institute of Medicine, 1999, pp. 5.]**

Executive summary conclusion: “ The psychological effects of cannabinoids, such as anxiety reduction, sedation and euphoria can influence their potential therapeutic value. Those effects are potentially undesirable for certain patients and situations and beneficial for others.”

**GRADE:** Convincing survey evidence that cannabis is used to decrease anxiety in some patients suffering from anxiety disorders.

**21. Cannabisprodukten im deutschen Sprachraum {The use of cannabis products in Germany} [Forsch Komplementarmed Suppl. S3: 1999, pp. 28-36.]**

170 subjects participated in an anonymous standardized survey. Questionnaires of 128 respondents were included. Most frequent mentioned indications for using cannabis were the following:

Depression (12%),  
Sleeping disorders (4.8%),

**GRADE:** Good, though slim survey evidence that Europeans use cannabis to reduce anxiety, assist with sleep and decrease depression.

**22. Summary of 2,480 medical marijuana patients interviewed by Dr. Tod Mikuriya [Submission to the Association for Cannabis Medicine.]**

This paper summarizes ICD classifications for diseases and categorizes the data according to mentions of cannabis use. The results indicate that: “2.9% of Dr. Mikuriya’s medical cannabis patients have a primary diagnosis of insomnia.” According to the table, 26% of his patients comprising 660 patients use cannabis for mood disorders including depression, anxiety disorder, attention deficit disorder, and panic disorder.

**GRADE:** This is excellent and extensive case-report evidence that cannabis is used by many persons to treat agitation, insomnia and depression.

**29. Insomnia-Personal Comments [Oerther: 1999.]**

This self-report describes the use of cannabis by a physician practicing medicine in an Evacuation Hospital in Vietnam in 1969. The author reports that cannabis assisted him with sleep. “ I enjoyed six or eight inhalations from a burning dispenser and followed with the first quiet dreamless, nightmareless solid uninterrupted eight hours of sleep in months. I had to get through another 2

suckass months of war, but as long as I was able to get my inhalations, I could sleep through the night.”

**GRADE:** Good evidence of a person working in Vietnam during the war who used cannabis to assist with sleep as well as decrease nightmares.

**31. [Delta-9] THC an an Hypnotic: An Experimental Study at Three Dose Levels [ Cousens, et. al., Psychopharmacologia (Berl.) 33: 1973, pp. 355-364.]**

THC was found to significantly decrease the time it took healthy insomniacs to fall asleep. Three dosage levels were tried with nine subjects tested once a week for six weeks. The most effective dose was the 20-mg. level.

**GRADE:** Good experimental evidence that cannabis has sedative properties.

**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:** There is sufficient evidence to justify including this disease or symptom of severe anxiety to the list. The MD should actively attempt to treat underlying issues, which may be contributing to insomnia, like stress, exercise and nutrition

***Submitted by:***  
***Edward Glick, RN***

***Date: March 28, 2000***

**Oregon Medical Marijuana Act**

## Debilitating Medical Conditions Advisory Panel Disease-Specific Recommendations

### AGITATION ASSOCIATED WITH ALZHEIMER'S DISEASE Research Review

#### 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**

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

**POSSIBLY**

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

**YES**

**Comments:** In relation to anti-psychotic medications and major tranquilizers cannabis is safe.

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

**YES**

**Comments:** For advanced Alzheimer's Disease symptoms the health benefits outweigh the risks by a large margin.

**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.*

**NO**

**Comments:** Alzheimer's disease is a progressive disease process with poor prognosis. The use of cannabis for this disorder is purely palliative.

**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.*

**YES**

**Comments:** Cannabis may improve the quality of life for the patient as well as caregivers considerably.

**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.*

[See general recommendations]

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

Summary of Findings

#### **1. Petitioner #1, petition and live interview**

The applicant is the wife of a man suffering from Alzheimer's dementia with an underlying anxiety state. She relays that cannabis:

"Has helped my husband to reduce the constant pacing and his uncooperativeness in the form of agitation. He is able to sit quietly without any anxiety after having marijuana."

The patient's physician has submitted the following note written in the comments section of an application to the OMMA:

"Pt has Alzheimer's Disease and associated agitation- MMJ relaxes him and controls agitation."

**GRADE:** Good self-report that cannabis smoking helps sedate the patient and results in decreased anxiety.

#### **8. Cannabis Use and Cognitive Decline in Persons under 65 Years of Age [Lyketsos, et. al., American Journal of Epidemiology, Vol. 149, No. 9: 1999, pp. 794-800.]**

This study analyzed 1,318 persons over time (12) years through the Mini-Mental State Exam. It concluded: "There were no significant differences in cognitive decline between heavy users, light users, and non-users of cannabis."

**GRADE:** Good epidemiological evidence that users of cannabis do not suffer from cognitive decline, although of limited relevance.

**15. Anxiety in the Elderly [Sheikh, et. al., The Psychiatric Clinics of North America Vol. 18, No. 4: 1995, pp. 871-883.]**

This is a good description of some of the underlying issues involved in managing people with a progressive incapacitating disease. There is no mention of cannabis.

**27. 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.]**

It describes a fluid extract of cannabis resins and 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.

**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)**

**Add symptom to list of symptom conditions pursuant to ORS 475.302(2) (b)**

**COMMENTS:**

There is no conceivable benefit from excluding a person with advanced symptoms of Alzheimer's Dementia from the list of conditions since this is palliative and no other concerns are relevant. The evidence that supports this is case studies, history of use and personal experience. There is no case-controlled literature.

**RATIONALE Re: this recommendation**

Please see general rationales.

***Submitted by:***

***Edward Glick, RN***

***Date: March 28, 2000***