

OREGON HEALTH DIVISION

ASSESSMENT WORKSHEET FOR EVALUATING PETITIONS TO EXPAND THE LIST OF "DEBILITATING MEDICAL CONDITIONS" UNDER THE OREGON MEDICAL MARIJUANA ACT

CONDITION ___ **BIPOLAR DISORDER** ___ DATE
REVIEWED ___ **3/25/2000** ___

I. Consideration of Available Evidence

Description of Evidence Considered:

1. "The Use Of Cannabis As A Mood Stabilizer Bipolar Disorder: Anecdotal Evidence And The Need For Clinical Research" by Grinspoon and Bakalar in the Journal of Psychoactive Drugs 30(2): 171-7, April-June 1998.
2. Case Reports in books by psychiatrists Lester Grinspoon, MD Marihuana: The Forbidden Medicine (1997 Yale University Press) and Tod Mikuriya, MD Marijuana Medical Handbook (1997 Quick American Archives) and from patient interviews.
3. Toxicity data comes primarily from the manufacturer's package inserts in the Physician's Desk Reference (PDR) and from several books in the Medical Cannabis Bibliography from website http://www.teleport.com/~omr/omr_mmj_bibliography.html including "Marijuana Myths: Marijuana Facts: A Review of the Scientific Evidence" by Lynn Zimmer, PhD & John Morgan, MD (1997 The Lindesmith Center).

Clinical Effectiveness (and comparison with established alternatives):

Controlled clinical trials are unavailable although there are many case reports reporting benefits of Cannabis as a mood stabilizer in bipolar disorder. Grinspoon & Bakalar use an analogy to lithium in the 1950's when its effect on mania had been discovered but there were no controlled studies.

Health Benefits and Risks:

Health Benefits include reducing manic episodes in some patients. The risks include sedation and potential pulmonary pathology if smoked. On the other hand, lithium, Tegretol, Depakote, and other mood stabilizers certainly have their risks as well.

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

For all patients (and their doctors), it is frustrating that there is no 100% effective mood stabilizer with a guarantee of an absence of side effects. Cannabis would certainly be a less attractive alternative than other choices for ALL patients but as Grinspoon & Bakalar demonstrate and as our patient interview demonstrates, there are "specific patient types" who benefit. Obviously, those are the patients for whom the benefits outweigh the risks. Specific patients may have received little benefit and/or high toxicity from more conventional drugs. In other words, Cannabis would be very low on the list of preferred medications because of a lack of controlled trials but a possible alternative when nothing else is acceptable.

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

Manifestations of Bipolar Disorder are variable and consist of a rather large spectrum of illness. In some, the manic phase may be the most disabling and in others the depressive phase may be the most disabling with or without a debilitating manic phase. Frequent cycling between extremes with disability from both phases represent an extreme level of seriousness. Current treatment of some patients remains unsatisfactory even under optimal treatment conditions. With this in mind, there are a subpopulation of individuals who will have a favorable impact from medical marijuana for this condition with improvement in net health and net overall impact.

Other Considerations:

Current treatments still result in patients entering general hospital emergency rooms with suicide attempts and/or violent episodes and/or having conflicts with law enforcement. One can only conclude that the current pharmacological treatment of bipolar disease does not produce consistently favorable results and new treatment alternatives may benefit patients.

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 [] Possibly [] No [**x**] NAD []

Comments:

The data is case reports.

(2) [A] **Clinical Effectiveness:** *The use of medical marijuana for this condition is clinically effective.* Yes [] Possibly [**x**] No [] NAD []

Comments:

Based on published case reports and patient interviews

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

Yes [] Possibly [] No [] NAD [**x**]

Comments:

A clinical trial comparing treatments and outcomes would be desirable but is not available.

(3) **Health Benefit/Risk Ratio:** *The health benefits of medical marijuana use for this condition outweigh the health risks.* Yes [] Possibly [**x**] No [] NAD []

Comments:

Bipolar disease is a serious mood disorder that can lead to death. Treatments are not uniformly effective and may have serious side effects. The PDR package inserts for lithium, Tegretol, and Depakote have "Black Box Warnings" stating that using the drug as directed may lead to death. The FDA approved THC/dronabinol/Marinol has no "Black Box Warning" in the PDR and no documented deaths in humans or lab animals have been demonstrated for marijuana overdose.

(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 [**x**] No [] NAD []

Comments:

For a small number of persons who have had an unfavorable response to standard therapy, Cannabis "might mitigate symptoms" of bipolar disorder.

(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 [] No [] NAD []

Comments:

Improvement in symptoms of severe bipolar disorder will have a favorable net overall outcome. Cannabis may possibly mitigate these symptoms.

(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 [] Possibly [] No [] NAD []

Comments: *(If yes, what are these issues and how do they alter these determinations?)*

In terms of lethality, Cannabis treatment is less toxic than standard anti-manic drugs like lithium, Depakote, & Tegretol. In the PDR, lithium, Depakote, & Tegretol carry "black box warnings" warning of possible death if used as directed. Importantly, this does not mean that Cannabis would be more effective as a treatment but it does mean that Cannabis treatment should result in less direct drug toxicity.

Note: NAD = Not Able to Determine

III. Overall Findings and Recommendations

Summary of Findings

Published case reports indicate that Cannabis can be an effective mood stabilizer for some patients but no controlled studies are available. Since the variability in the course of bipolar disease is so dramatic and the response to medication (including toxicity) is so unpredictable (for example, who will get agranulocytosis and die from Tegretol/carbamazepine and who will develop neurological and/or metabolic complications from lithium and who will get liver failure from Depakote/divalproex), Cannabis may have a role as an alternative treatment when certain criteria are met.

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) [X]

Do NOT add disease or symptom to list of debilitating medical conditions []

COMMENTS Re: this Recommendation:

If it were possible to add "severe symptoms of bipolar illness" with "severe" meaning that other treatment options have failed or been toxic, this would be my preference. Another synonym for "severe" in this setting might be "refractory". "Severe bipolar disease with unfavorable response to conventional treatment" would also summarize my recommendation.

RATIONALE Re: this Recommendation:

Listing as a symptom is a softer recommendation than adding this as a disease because the data consists of compelling case reports rather than controlled trials. Dr. Grinspoon may be correct that Cannabis treatment for certain patients under certain circumstances may be similar to the situation involving lithium treatment in the 1950's.

Strength of this Recommendation:

Without placebo controlled double-blind trials of Cannabis versus placebo versus lithium versus Tegretol versus Depakote, etc. the recommendation is somewhat soft. On the other hand there are numerous published case reports that indicate benefit for some patients and the toxicity of the more commonly used mood stabilizers are significant.

Other Comments, Observations, Etc

It would be unfortunate to deny patients and doctors this opportunity to help someone with a potentially fatal illness that often is very difficult to manage. In addition, the standard medication used to treat the manic phase of bipolar illness can be fatal if taken as directed while Cannabis is not. The benefit to risk ratio may be quite favorable for someone who has had an unfavorable response to alternative more conventional treatments, especially if that unfavorable response included toxicity.

Submitted By:

Signature

Print Name