

Oregon Medical Marijuana Act Debilitating Medical Conditions Advisory Panel

Bipolar (Depressive and Other Mood Disorders) Research Review

NOTE: Bipolar and mood disorders generally include anxiety disorders. Anxiety disorders will be evaluated in a subsequent review. An attempt has been made to select information for this review which pertains to bipolar disorder; however, a large amount of material classifying all mental disorders together, as relating to substance use and dependence issues, has been included in the Psychotic Disorders Review and will not be repeated here. Also, since schizophrenia and psychotic disorders were the primary focus of testimony before the advisory board they will not be repeated here.

1. CONSIDERATION OF EVIDENCE

Description of Evidence Considered:

1. **Substance Abuse and Bipolar Comorbidity [Sonne, et. al] The Psychiatric Clinics of North America Newsletter, Vol.22, Number 3, 1999.]**

Literature survey describing the high association between bipolar disorder and substance use issues. It repeatedly emphasizes cocaine and ETOH as associated features with bipolar disorder. No mention of cannabis as comorbid feature with severe effects- (unlike cocaine, ETOH.)

GRADE: Good evidence to conclude cannabis is not major contraindication to bipolar disorder as documented in this study.

2. **DSM-4 Diagnoses associated with class of substances, [Diagnostic and Statistical Manual of Mental Disorders, 4th ed., pp177.]**

A one-page table compares major mental illnesses with associated substances including cannabis. It indicates that cannabis use is not associated with mood disorders.

GRADE: Good evidence that cannabis is not categorically contraindicated in persons suffering from bipolar disorder based upon associated substances of abuse.

3. **Petitioner submission and interview**

The petitioner states in his written submission that he has a family history of bipolar disorder including his younger sister. He also appears to suffer from

Attention Deficit Disorder because “... could not concentrate more than a few seconds at a time.” The petitioner was hospitalized several times, beginning at the age of 20 for symptoms of dangerousness and impulsiveness and “was on many drugs-prescribed.” The letter from petitioner’s parents says:

“We told him we did not approve [of cannabis use] and not to do it around us. He hasn’t used it around us and never looks as if he is using it. He has been working and supporting his family every day since 1988.”

Notes from the petitioner’s physician state:

“ Since 1987 Mr. ____ has not had a full blown manic episode. He quit taking lithium and psychoactive drugs and has treated his disorder with cannabis exclusively since 1988. The only time during the last eleven years that he has felt that he was getting manic was when he quit using cannabis.”

GRADE: Reliable self-report and physician report that petitioner has been using cannabis for many years to control the symptoms of his bipolar disorder with minimal indications of harm.

4. Cannabis- THC and Bipolar Disorder (Included with patient’s petition) Marijuana and Medicine: Assessing the Science Base [Institute of Medicine, 1999.]

A. Describes the action of cannabinoids at cellular level as consistent with those that would decrease mania. (See petition notes)

B. Describes side-effect profile as “within the range tolerated for other medications.”

GRADE: Good evidence that cannabis side effects fall well within acceptable range. Fair evidence that cannabis reestablishes neurotransmitter balance in some manner that decreases manic symptoms

Clinical Effectiveness (and comparison with established alternatives)

The research base indicates that cannabis may have mood stabilizing effects in a sub- population of individuals. Evidence indicates that established alternatives (Lithium, Depakote, Tegretol) carry significant risks including risk of congestive heart failure, nausea, diarrhea, aplastic anemia, thrombocytopenia, hepatitis, Stevens-Johnson Syndrome, cardiac arrhythmias, renal toxicity, hyponatremia, tinnitis, lithium toxicity, pancreatitis, anorexia and death. Clinical literature indicates no lethal dosage of cannabis.

Health Benefits and Risks:

The health benefits of cannabis for bipolar disorder are minimally understood but generally relate to its anti-anxiety effects, which perhaps allow bipolar patients to reflect on their behavior by increasing insight and decreasing impulsiveness. No clinical research has been done to my knowledge that describes this action;

therefore the evidence base is circumstantial and mostly composed of case-reports. The health risks of cannabis use are more clearly understood as they relate to bipolar disorder. Cannabis may cause a paradoxical reaction, which increases mania and agitation and decreases insight. Research reviews indicate that some significant percentage of persons with bipolar disorder have underlying substance dependence disorders which may be exacerbated by cannabis use. There is survey evidence that cannabis may precipitate hallucinations in bipolar persons but the etiology of this association is unclear. Bipolar disorder carries with it significant risk of violent death. The benefits of cannabis may outweigh this lethal outcome for some percentage of users who are not refractory to it.

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

Factors that affect safety are the legal proscriptions in Federal law, which classify virtually ALL cannabis use as a crime. Thus, bipolar patients may be at greater risk for harm through violent associations with police those operating illegal drug networks. Factors affecting effectiveness are reviewed above.

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

Net health impact appears variable for different patient populations. For an unknown but significant percentage of bipolar cannabis-using persons the net impact is positive. The association between bipolar disorder and comorbid substance appears confounded by the inclusion of alcohol and cocaine in the survey results. Thus, it is far from clear that cannabis is uniformly contraindicated in persons who suffer from bipolar disorder, based upon this evidence. The petitioner convincingly presents at least one instance where bipolar symptoms are treated successfully by cannabis with a clear net positive result. Historical literature presents many other instances. Unfortunately, research has not been conducted to explore this positive association, thus it is impossible to extrapolate from this one convincing report.

Other Considerations

[None]

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 clearly a lack of clinical research evidence to describe why a percentage of cannabis-using bipolar patients are effectively controlling their symptoms with cannabis, only that they are, in fact, doing so.

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

NAD

Comments:

There is clear though sparse evidence of clinical efficacy for some small percentage of cannabis-using persons with bipolar disorder.

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

POSSIBLY

Relative clinical effectiveness measured in comparison to established drug regimes indicates efficacy.

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

NAD

Comments: Although benefit/ risk analysis for the petitioner clearly indicates a net benefit it is unknown to what extent this may be extrapolated into the bipolar population as a whole, since there is some evidence that cannabis use may complicate the course and severity of bipolar disease.

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

Comments: As with #4 above the evidence is inconclusive regarding the extent to which cannabis may be a successful treatment for bipolar disorder. The petitioner clearly benefits from using it. What is clear is a high mortality rate either by homicide or suicide of persons who suffer from bipolar disease, and that standard drug therapies are associated with sometimes severe or life-threatening side effects. Cannabis does not appear to contribute to mortality rates.

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: The net overall impact when compared with standard drug regimes appears positive for a small percentage of bipolar patients, especially those who

are refractory to more conventional treatments or those who do not have severe comorbid substance use problems.

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

The issue of the legal status of chronically ill people alters these determinations in the following way: The United States government has followed a policy of hindering research into the potential therapeutic uses of cannabinoids for nearly six decades. This policy, which continues today make serious clinical research extremely difficult to pursue, and has been called “Byzantine and demeaning “ by Ethan Russo, one of America’s preeminent researchers into the utility of cannabinoids. 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. The continuing Federal policy of obstruction has created a situation where high-grade evidence of clear medical utility in persons suffering from bipolar disorder is nearly impossible to obtain or corroborate. Until this research is allowed to proceed it is indefensible on humanitarian grounds to forbid access to cannabis for patients who are under a physician’s care and who suffer severe symptoms. 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 harm to ill people than their use of cannabis.

III. Overall Findings and Recommendations

Summary of Findings

This evidence base consists of the following information:

One (1) petitioner report, which indicates substantial benefit from the regular use of cannabis along with strong corroboration by this person’s physician;

One (1) research survey which indicates that alcohol and cocaine use are implicated in poor outcomes with bipolar patients, but which indicates that cannabis is low on the list of causative factors which complicate the treatment of bipolar disorder;

One (1) table from the DSM-4 which indicates that cannabis is not indicated as a primary complicating factor in persons suffering from bipolar disorder.;

One (1) article titled: “Cannabis- THC and Bipolar Disorder” (Included with patient’s petition) including a quote from Marijuana and Medicine: Assessing the Science Base[Institute of Medicine], 1999

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:

Based upon this evidence there is slim experimental evidence that Cannabis is a “first-line” treatment for bipolar disorder. (It is worth noting that the petitioner has exhausted his medical alternatives and is prevented from accessing the medical establishment more fully because of financial limitations.) There is good evidence that the petitioner is gaining great relief from his use of cannabis based upon his physician’s assessment as well as the fact that he has remained non-hospitalized since his use began 10 years ago. It appears that Cannabis has managed the manic phase effectively after many unsuccessful medication trials. The side-effect profile is well within acceptable range. It is reasonable to extrapolate from the petitioner’s experience to conclude that there are a significant number of Oregonians who may benefit from medically monitored cannabis use

RATIONALE Re: this recommendation

This patient, who suffers from the serious and potentially lethal complications of bipolar disorder, faces potentially grave harm of injury or death because of the Federal ban on the use of cannabis. He, and other’s who successfully use cannabis, face the prospect of arrest, prosecution, and incarceration by Oregon law enforcement agencies because of this use. Therefore those who suffer from bipolar illness and are under the care of a primary care provider, should be allowed legal access to the Marijuana Registry Program with the following suggested provisions:

- A. The patient should be refractory to more conventional treatments (Lithium, Tegretol, Depakote);***
- 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;***
- D. The MD should consider “N- of-1” research evaluations; and,***
- E. The MD should carefully evaluate hepatic and neurochemical interactions with initiation of pharmacotherapy.***

NOTE: The negative consequences of patient involvement in illegal drug networks are a significant threat to bipolar patients who sometimes lack impulse control functions. Additionally, state law-enforcement resources are misdirected if bipolar patients come into contact with police as a result of impulsivity and lack of insight. This creates potentially dangerous situations for the manic patient and police. It also diverts law-enforcement resources from more important and basic public health protection.

A symptom-based designation for inclusion of severe anxiety /agitation may adequately address manic and hypo-manic episodes.

Submitted by:
Edward Glick, RN

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