This document is made available electronically by the Minnesota Legislative Reference Library as part of an ongoing digital archiving project. http://www.leg.state.mn.us/lrl/lrl.asp

Petitions to Add Qualifying Medical Conditions to the Medical Cannabis Program

A REPORT TO THE COMMISSIONER OF HEALTH

October 27, 2016

Medical Cannabis Review Panel

FOREWORD

This report was produced by the medical cannabis citizens' review panel established under Minnesota Rules part 4770.4003, subpart 3. The report was written by the panel members, with administrative support from the Minnesota Department of Health.

Members of the Review Panel participating in this report were:

Heather Tidd, chairperson (Patient Advocate)
Dr. Susan Sencer, MD (health care practitioner with pediatric expertise)
Mikel Bofenkamp, Pharm.D. (member at large)
Dr. Andrea Hillerud, MD (member at large)
Elizabeth Melton, JD (member at large)
Dr. George Komaridis, Ph.D., LP (member at large)

A seventh member, Dr. Pamela Gonzalez, MD (health care practitioner), was unable to participate.

The Review Panel's report to the Commissioner of Health must include potential public health benefits and risks of adding or rejecting a medical condition petitioned for inclusion on the list of medical conditions that qualify a person's enrollment in the medical cannabis patient registry program.

The Commissioner of Health will consider this report, any available evidence-based, peer-reviewed research that medical cannabis will provide therapeutic benefit, and other potential therapeutic factors in reaching a decision regarding whether to add a qualifying medical condition petitioned for the medical cannabis patient registry program.

Contents

Introduction

This Review Panel was appointed by the Minnesota Department of Health (MDH) to review petitions requesting the addition of qualifying medical conditions for the Minnesota medical cannabis program. The Panel's responsibility is to report on potential public health impacts, including therapeutic factors and known potential benefits and risks of using cannabis to treat the petitioned medical conditions.

The Panel met four times. It received public testimony at two of the meetings and was given copies of written comments received by MDH. The Panel heard testimony about acquired absence of limb, autism, diabetes, and schizophrenia at its September 8, 2016 meeting. It heard testimony about arthritis, Ehlers-Danlos Syndrome (EDS), insomnia, treatment-resistant depression, and Post-Traumatic Stress Disorder (PTSD) at its September 22, 2016 meeting.

The Panel heard persuasive public testimony about the potential of cannabis to treat some of these conditions and received written comments from people who suffer from them. In addition, the Office of Medical Cannabis produced an "issue brief" reviewing scientific studies involving each petitioned medical condition. There is little scientific data, in the form of gold-standard, clinical research studies, about the efficacy of cannabis in treating these medical conditions that would corroborate the oftentimes persuasive public testimony about the efficacy of cannabis to treat these conditions.

Many of the potential harms of using cannabis to treat medical conditions are shared by all the petitioned conditions. These include concerns about negative effects on developing brains, use by pregnant or breastfeeding women, and use by those with a family history of psychosis. Other public health concerns include the potential increase in people driving while impaired by cannabis. Although there is an addictive potential for cannabis, the literature says only about 5% of chronic cannabis users become addicted.

These potential harms need to be weighed against the potential harms of treatments currently available to these patients. For example, many of the chronic drugs given to children with seizures or autism also have negative cognitive effects and addiction concerns. There are similar concerns with medications to treat the other diagnoses as well

One concern is over the unknown long-term effects of the cannabis extract products used in the Minnesota medical cannabis program, even the low-THC products. At this point, there is not sufficient data to say what these long term effects could be. The concern is heightened when talking about children.

Although outside the scope of the Panel's charge, we heard from many people who believe whole plant cannabis products are more effective than the extract products available through the medical cannabis program due to the "entourage effect."

The Petitions

Acquired absence of limb/phantom limb pain

This petition is about managing the pain associated with acquired absence of a limb. Cannabis may be a helpful treatment modality. Patients with intractable pain due to acquired absence of limb would currently qualify for the program, however several patients told us that because acquired absence of limb is not an option on the intractable pain drop down menu that their providers would not approve it. If it is not added as its own condition, perhaps it could be added to the menu so that providers would feel more comfortable with allowing it as intractable pain.

The Panel reviewed the petition and the issue brief prepared by the Office of Medical Cannabis. There was no public testimony about this condition and only one written comment received from someone without direct knowledge of the use of cannabis to treat pain associated with acquired-absence of limb.

Even though medical cannabis can currently be used to relieve intractable pain associated with this condition, the Panel could justify it being added as its own qualifying medical condition and not simply as a subset of Intractable Pain because cannabis might also help reduce anxiety and other symptoms associated with phantom limb pain.

Arthritis

The Panel reviewed the petition to add arthritis and the issue brief prepared by the Office of Medical Cannabis. Four persons testified about the effects of cannabis on this condition and two written comments were received from people with direct knowledge of using cannabis to treat their arthritis pain. The patients that were currently using cannabis for their arthritis pain reported that it provided pain relief which allowed them to have a healthier more active lifestyle and participate more often in their physical therapy resulting in better health overall.

Even though the petition is primarily focused on pain relief, there are some indications that medical cannabis could work on multiple symptoms of arthritis, including inflammation (especially for rheumatoid arthritis) and interrupted sleep. Medical cannabis potentially could do more than just alleviate pain symptoms and could be a disease-modifying rheumatologic drug. More research is needed, however.

Existing treatments for arthritis sufferers are not very effective and can have serious side effects. Cannabis seems to have lesser side effects than pharmaceutical medications prescribed for arthritis sufferers.

Autism Spectrum Disorder (ASD)

There was significant interest shown in autism. In addition to the petition and issue brief, the Panel received public testimony from three persons and ten written comments from people supporting adding autism as a qualifying medical condition. The comments in opposition to adding it came from those opposing adding any psychiatric qualifying medical condition and were not specifically addressed to merits or risks of using medical cannabis to treat those with autism.

There was compelling public testimony about the impact this condition has on families and details about how the symptoms of this disorder affect the patient's entire family. Family members shared remarkable stories about the success they've had using cannabis to help their autistic child. These successes not only impact the child but impact the family by alleviating some of the symptoms and generally improving the patient's (and family's) quality of life. The Panel also heard that when the patient becomes an adult s/he frequently needs to move into group home; this is costly both from a monetary perspective and also an emotional one. If these patients are able to have more controlled and calm behavior with cannabis they would likely be able to live with their families much longer and stay active members in the community.

As with almost all the petitioned conditions, hard scientific data regarding the use of medical cannabis is hard to find. There is, however, a wealth of anecdotal and observational evidence that cannabis seems to alleviate anxiety, help with social interactions, help with impulse control, reduce aggression, allow the child to improve academically, increase appetite, help with toileting, and help keep the child in the home. One testifier explained, "it just slows them down somehow," which is often needed for these children.

The primary risks of adding autism as a qualifying medical condition are concerns about the effects of cannabis on developing brains and impacts on cognition and greater potential for developing dependence when use starts at an early age. However, most of these children are already on powerful psychotropic drugs which also have broad negative consequences.

Patients with autism do have a higher suicide rate and early death rate, often due to their mental health and impulsivity issues. If cannabis can help their anxiety and help with their impulsivity it may lower those risks and lead to longer lives. It is important to remember that while we heard testimonies only about children, adults also have autism and it is likely the cannabis would help them in similar ways.

The bottom line is that families in this situation do not have great options. These families are looking for hope. Autism affects a patient's entire family. The commissioner should consider that these families do not have better options or treatment plans for their children with autism. If autism is included as a qualifying medical condition, it could be beneficial for the families and community.

Depression, treatment resistant

Treatment-resistant depression does not have a clinical definition, but can be thought of as a subset of major depressive disorder that does not respond to currently accepted treatments. The Panel reviewed the petition, issue brief drafted by the Office of Medical Cannabis, four persons testified at a public hearing about how their cannabis use has affected their depression generally, and the Panel received two written comments related to treatment-resistant depression.

Medications commonly used to treat depression have more harmful side effects than cannabis does. People with severe depression are more likely to have benefit from medications currently available to them than are people with less severe depression and newer anti-depression medications have fewer negative side effects than medications that have been around longer. The Panel heard testimony that cannabis is the only thing that "gets me out the door." Some people with depression do seem to benefit from cannabis. On the other hand, there is a concern that medical cannabis could worsen the depression by increasing the lack of motivation, feelings of isolation, and desire to avoid interaction with others.

If the commissioner considers adding treatment resistant depression as a qualifying medical condition, the emphasis should be on "treatment resistant." If nothing else is working to treat a person's depression, then why not let them try cannabis? For example, in the case of depression with catatonic features, it might be good to try cannabis before such potentially harmful treatments as electro-convulsive therapies, which can cause pain, nausea and memory loss.

Diabetes (blood sugar control)

Diabetes is a chronic disease with significant health care and public health costs. The Panel reviewed the petition, the issue brief drafted by the Office of Medical Cannabis, heard public testimony from one person, and received three written comments. There are some clinical studies that warrant further study.

There is some scientific support for cannabis having an impact on blood sugar control. There are theoretical and preclinical data that the endocannabinoid system is involved with metabolism, insulin sensitivity and possibly insulin production. There are also epidemiological studies that non-diabetic marijuana users have a lower BMI and higher insulin sensitivity than non-diabetic non-users.

Two studies conducted by GW Pharma of CB1 receptor antagonists that work with the endocannabinoid system are relevant. The first and most directly relevant study is a recently published a trial of the cannabinoids THCV (or tetrahydrocannabivarin), CBD (or cannabidiol) and various combinations of the two versus a placebo in humans with type 2 diabetes. This study showed THCV improved glycemic control but CBD did not. It should be noted that even

though THCV is a cannabinoid that is not currently regulated or tracked in Minnesota's medical cannabis program, the state registered medical cannabis manufacturers could develop products high in THCV.

The second study was of GW Pharma's anti-obesity drug Rimonabant, which is also a CB1 receptor antagonist. This study, although not about diabetes, could also support the plausibility that cannabinoids that are CB1 receptors antagonists may be a useful treatment for diabetes.

The Panel heard specific testimony of cannabis working for a person with diabetes and how cannabis helps their body do what it is supposed to do and the pancreas to work like it is supposed to work. The cannabis does more than simply mask the symptoms. Medical cannabis could be used to reduce weight gain (as was the case in the testimony we heard), regulate appetite, and regulate insulin levels. Health care expenses could go down for their current medications and their quality of life would likely improve.

The bulk of epidemiological data would point toward medical marijuana used to treat type 2 diabetes via decrease in BMI and possibly an increase in insulin sensitivity. There is less evidence for the use of marijuana or medical cannabis to treat type 1 diabetes.

Ehlers-Danlos Syndrome (EDS)

Ehlers-Danlos Syndrome (EDS) is a group of inherited connective tissue disorders. The Panel reviewed the petition, the issue brief drafted by the Office of Medical Cannabis, heard public testimony regarding EDS and cannabis from six persons, and received one written comment about EDS.

There is currently no cure for EDS. There are not many medications or treatments available to patients. The focus is on pain management. Medical cannabis could reduce pain associated with EDS. Cannabis could also reduce inflammation, help with insomnia, arthritis, depression and regulate appetite. There was also public testimony that medical cannabis might also have preventative effects on EDS.

The only treatment plan for EDS is to build muscle, but the pain that comes from this process can be too much for people. Patients currently using cannabis testified that it can be used to manage pain, which in turn helps them do the needed physical therapy and exercise to build muscle.

EDS is not a "large" medical condition with a great number of people suffering from it. Big pharmaceuticals are not as likely to invest resources to develop a medication to help these patients. Medical cannabis is an option.

EDS patients do not have good treatment options without medical cannabis. The Panel is concerned that if EDS is included only as a subpart of Intractable Pain, those who suffer from it may not realize they are eligible for the program. Since cannabis can also help with the insomnia, appetite and depression associated with EDS we feel that making EDS a stand-alone qualifying medical condition could be justified.

Insomnia

The Panel reviewed the petition to add insomnia, the issue brief drafted by the Office of Medical Cannabis, heard testimony from four people about their experiences, and received two written comments.

There are multiple clinical trials that suggest cannabis can benefit sleep. In general, these trials are less than ideal because they measure sleep as a secondary outcome in patients with other medical conditions. These trials have also been conducted with multiple forms of cannabis, not all consistent with products available in the Minnesota medical cannabis program. Medical cannabis may or may not be more effective than prescription medications available.
The case for adding insomnia as a qualifying medical condition is stronger if cognitive behavioral therapy has failed the patient. The efficacy of current prescription drugs for insomnia is not that great and they also carry risk of harm.

Pharmacotherapies for insomnia may cause cognitive and behavioral changes and may be associated with infrequent but serious harm. Prescription benzodiazepines and non-benzodiazepine sleep aids are typically used to treat insomnia and are somewhat effective; anecdotal evidence suggests that medical cannabis is also effective. One potential benefit of medical cannabis is that it does not have the “groggy-morning” after effect that many insomnia medications have, obviously most people need to be alert in the mornings and this is a concern for them. It would be reasonable for a patient to want to try medical cannabis to treat insomnia prior to a prescription benzodiazepine on nonbenzodiazepine. Some panel members have concerns that insomnia is a subjective disease and is therefore open to manipulation and abuse. DSM-V criteria for insomnia includes:

> Dissatisfaction with sleep quantity or quality, with one or more of the following symptoms: difficulty initiating sleep, difficulty maintaining sleep, early-morning awakening. It is hard to detect insomnia, hard to separate a condition. It is all based on self-reporting.

On the other hand, the subjective nature could be looked at as a reason to approve. If Insomnia is added as a qualifying medical condition, patients could determine whether they are satisfied with medical cannabis as a treatment on their own, and with the aid of global outcome measurement provided by cannabis centers. Efficacy could be measured by Insomnia Severity Index or Pittsburgh Sleep Quality Index. We could even compare efficacy down the road to

prescription drugs. Evaluation of this data could allow a comparison of medical cannabis and prescription drugs.

The Panel suggests that if insomnia is added as a qualifying medical condition, it should be allowed only after other treatment alternatives have been tried by the patient and are found to be ineffective.

Post-Traumatic Stress Disorder (PTSD)

Post-Traumatic Stress Disorder (PTSD) became a DSM diagnosis in the late 1970s for the purpose of clarifying the psychological effects of trauma on humans. It was originally described as one type of anxiety disorder, but it has been given its own diagnostic status in DSM-V. The Panel reviewed the petition and its attachments, the issue brief drafted by the Office of Medical Cannabis, heard public testimony from nine people, and received 20 written comments.

In order to meet the DSM-V criteria for a PTSD diagnosis, an individual must meet a number of criteria (these are described in the attached Issues Brief). It is a complicated disorder that is slowly becoming better understood. Medication is often used as an adjunct to cognitive and desensitization therapies in the treatment of PTSD, understanding that it can help an individual who is working through the therapeutic processes. Some patients are treatment resistant or choose not to become involved in psychotherapeutic procedures. Whatever the reasons, outcomes from available medications have been poor and multiple medications, with harmful side effects, are typically prescribed to patients.

The Panel heard from the public, including veterans, who are currently using cannabis to treat PTSD. They report they are far less aggressive or prone to rages and that cannabis helps with falling asleep and sleeping through the night. One veteran shared that he no longer calls the suicide hotline weekly, that his mental health is greatly improved and he can now participate fully in therapy. It was heard repeatedly that cannabis has fewer and less bothersome side effects than other medications. A recent study found that 20 Veterans commit suicide each day, we heard testimonies saying that cannabis helped reduce suicidal ideations. Currently 14 states allow cannabis as a treatment for post-traumatic stress disorder.

The Panel heard from many sources that current medications are not effective and medical cannabis has the potential to increase the quality of life for people suffering with PTSD. Some form of medication is likely to be used to assist treating patients with PTSD. The promising effects of medical cannabis for PTSD victims appear to be more potent and less harmful than existing pharmaceuticals. There is a feeling of responsibility to help the people who have fought for us, certainly we should give them every option to be healthy.

Schizophrenia

Schizophrenia is a cognitive disorder and is difficult to treat. The Panel reviewed the petition and the issue brief drafted by the Office of Medical Cannabis and received one general written comment and a statement from two professional organizations that oppose the addition of any psychiatric conditions as a qualifying medical condition for the medical cannabis program. No public testimony was presented to the Panel concerning cannabis as a treatment for schizophrenia.

Psychotherapy is not very effective for treating schizophrenia and anti-psychotic medications are typically used. These medications have strong, frequently harmful side effects and they rarely cure the patient (often the patients are on anti-psychotic medications for life). Any treatment option with fewer harmful side effects would be beneficial.

Medical cannabis may have an effect on cognitive processing, however there has not been a lot of research in this area. It seems from the literature that the cannabinoid THC can actually cause more psychotic-type episodes; the cannabinoid CBD, on the other hand, seems to have psychotic reducing effect. The science has not developed to a point of providing a clear picture. This condition raises the most concern among Panel members because of the potential to cause or increase psychotic reactions. If it were adopted, the patients would need to be very closely monitored. There are worries about allowing these patients a 30-day supply of cannabis and leaving them unmonitored until their next visit to a Cannabis Patient Center.