MDH Minnesota Department *of* Health

Minnesota Medical Cannabis Program
Petition to Add a Qualifying Medical Condition

Section A: Petitioner's Information

Name (First, Middle, Last): [redacted]			
Home Address (including Apartment or Suite #): [redacted]			
City: [redacted]		State: MN	Zip Code: [redacted]
Telephone Number: [redacted]	E-mail Address: [redacted]		

Section B: Medical Condition You Are Requesting Be Added

Please specify the name and provide a brief description of the proposed qualifying medical condition. Be as precise as possible in identifying the condition. **Optional:** Include diagnostic code(s), citing the associated ICD-9 or ICD-10 code(s), if you know them. *Attach additional pages as needed.*

See attached.

MDH Minnesota Department *of* Health

Minnesota Medical Cannabis Program
Petition to Add a Qualifying Medical Condition

Section C: Symptoms of the Proposed Medical Condition and/or Its Treatment

Describe the extent to which the proposed qualifying medical condition or the treatments cause suffering and impair a person's daily life. *Attach additional pages if needed.*

See attached.

Section D. Availability of conventional medical therapies

Describe conventional medical therapies available and the degree to which they ease the suffering caused by the proposed qualifying medical condition or its treatment. *Attach additional pages if needed.*

See attached.

MDH Minnesota Department of Health

Minnesota Medical Cannabis Program
Petition to Add a Qualifying Medical Condition

Section E: Anticipated benefits from Medical Cannabis

Describe the anticipated benefits from the medical use of cannabis specific to the proposed qualifying medical condition. *Attach additional pages if needed.*

See attached.

Section F (optional): Scientific Evidence of Support for Medical Cannabis Treatment

It will strengthen your petition to include evidence generally accepted by the medical community and other experts supporting the use of medical cannabis to alleviate suffering caused by the proposed medical disease or its treatment. This includes but is not limited to full text, peer-reviewed published journals or other completed medical studies. Please attach complete copies of any article or reference, not abstracts.

☒ ***I have attached relevant articles.*** *(check box if you have attached scientific articles or studies)*

Section G (optional): Letters in Support of Adding the Medical Condition

Attach letters of support for the use of medical cannabis from persons knowledgeable about the proposed qualifying medical condition, such as a licensed health care professional.

☐ ***I have attached letters of support.*** *(check box if you have attached letters of support)*

MDH Minnesota Department of Health

Minnesota Medical Cannabis Program
Petition to Add a Qualifying Medical Condition

Section H: Acknowledgement and Signature

Please Note: Any individually identifiable health information relating to any past, present, or future health condition or health care contained in this Petition is classified as a health record under Minnesota Statutes §144.291, and is not subject to public disclosure.

I certify that the information provided in this petition is true and accurate to the best of my knowledge.

SIGNA [redacted] DATE (mm/dd/yyyy) 7/26/18

To obtain this information in a different format, call:
(651) 201-5598 in the Metro area and (844) 879-3381 in the Non-metro.

Petition for Psoriasis

B. Medical Condition You Are Requesting Be Added

This petition proposes that psoriasis be recognized as a qualifying condition to receive medical cannabis under subdivision 14 of the Minnesota Statues section 152.22. Psoriasis can be classified as Psoriasis vulgaris (ICD-10-CM L40.0), Generalized pustular psoriasis (ICD-10-CM L40.1), Guttate psoriasis (ICD-10-CM L40.4), other psoriasis (ICD-10-CM L405, L40.8), and unspecified psoriasis (ICD-10-CM L40.9).

Psoriasis is a noncontagious and chronic inflammatory skin disease that produces plaques of red, thickened, and scaling skin most commonly affecting the elbows, knees, and scalp.[1] The dry flakes of skin result from the excessive rapid proliferation response of keratinocytes triggered by inflammatory chemicals produced by T-lymphocytes. Symptoms of psoriasis can fluctuate and at intermittent intervals may spontaneously get better or worse. While psoriasis is not curable, it can go into remission at which times the skin appears normal and is clear.

Under the broader diagnosis of psoriasis, there are 5 different types of skin conditions.[1] The most common type of psoriasis is plaque psoriasis, followed by inverse psoriasis, guttate psoriasis, pustular psoriasis, and the rarest type, erythrodermic psoriasis.[1] Symptoms of the psoriatic condition will depend on the exact subtype. Patients with psoriasis may have more than one type or different types of psoriasis at different times throughout their lifetime.

C. Symptoms of the Proposed Medical Condition and/or its Treatment

According to the National Psoriasis Foundation, more than 8 million Americans suffer from psoriasis and worldwide it is seen in 125 million people.[1] The most common symptom of those with psoriasis are thick scaly patches, also known as plaques, that develop on the surface of the skin, affecting about 80% to 90% of those with psoriasis.[2] Plaques can vary in size and can appear anywhere on the body, but most commonly are found on the knees, elbows, and scalp.[3] The discomfort and itching that comes as a result of the red, thick, scaly patches on the skin can become so detrimental it can prevent a person from carrying out daily activities and reduce their quality of life. On top of the pain and itchiness experienced by psoriasis sufferers, the visible appearance of their skin can be equally detrimental due to social stigma and lowered self-esteem.[4] Furthermore, those impacted by psoriasis may develop depression, anxiety, and suicidal ideation, even in cases of mild psoriasis. [4] In an article by Feldman et al., it was estimated that the economic burden of the disease on both the patient and society, was estimated at $112 billion in 2013.[2] This included both direct costs, estimated at $63.2 billion, and indirect costs (such as loss of productivity at work), which was estimated at $35.4 billion.[2]

As the tolerability of each of the therapy options is different and often individualized, some or all of these remedies may not work. People with psoriasis have a higher risk of developing lifelong co-morbidities, especially when left untreated, which includes hypertension,

hyperlipidemia, cardiovascular disease, inflammatory bowel disease, liver problems, psoriatic arthritis, obesity, metabolic syndrome, and depression.[1,3,6] Over time, these untreated psoriasis skin changes can cause unnecessary stress to the affected individual and can lead to other health problems that lead to comorbidity evaluations in the state's emergency room and sizeable numbers of hospital admissions thereby putting additional strain on the healthcare system.

D. Availability of conventional medical therapies

Studies have shown that psoriatic care is far from acceptable as many treatments have a low rate of success, have marked side effects, and are not cost effective.[4] Conventional therapies to treat psoriasis range from the use of biologics, oral treatments, phototherapy, and topical applications to lifestyle choices such as a change in diet or introduction of vitamins and supplements. This section of the petition will provide a short description on each of the above and a current issue surrounding that particular treatment option.

- Biologics are medicines made from complex molecules manufactured using living microorganisms, such as human, animal, or bacterial cells that are given through injection or intravenous infusion. [8] Biologics work to target specific parts of the overactive parts of the immune system to reduce inflammation. [1] Currently, there are six biologic drugs approved by the FDA to treat moderate to severe psoriasis. Biosimilars are like biologics in how they treat psoriasis by suppressing the overactive immune system, however fall under a different classification as they are not exact copies of the biologic version. Both biologics and biosimilars carry a hefty price tag and are not offered in a generic version. While the cost may be lower for those with medical coverage, for those who are uninsured these medications can cost anywhere from $2,000 to $6,000 per month. A price increase to Humira (adalimumab), a widely used biologic for psoriasis, is projected to add $1.2 billion dollars of cost to the US health care system.[9] Furthermore, there are disadvantages pertaining to the use of biologics, which includes possible development of allergic reactions to latex, the risk of serious infection, and a limited safety experience.

- Oral treatments, that come in oral liquids or a pill form, also target specific cells of the immune system to decrease over activity. [10] These treatments can carry side effects of serious infection, liver problems, kidney problems, and in some cases may cause birth defects.[7]

- Phototherapy is a specific type of treatment that utilizes certain types of light to slow rapidly growing skin cells, slow the overactive immune system, and reduce inflammation. [10] Phototherapy is primarily given under the supervision of a health care provide and due to the frequency of phototherapy sessions, ranging from 3-5 times per week for an average time period of 6 months to a year, it can be a demanding and inconvenient option for many. Furthermore, the side effects of light therapy can include burns, blisters, hyperpigmentation, and a possible risk of non-melanoma skin cancers.[10]

- Topical applications are also used for the treatment of psoriasis and come in the form of creams, lotions, and sprays. For moderate to severe cases of psoriasis larger proportions of the body may be affected and therefore it may not be practical or effective to treat in a topical manner.

E. Anticipated Benefits from Medical Cannabis

Psoriasis is a difficult disease to treat. First-line therapies can be effective for many patients, and completely ineffective for others. Many patients face a lifelong struggle to effectively treat their psoriasis. Medical cannabis would provide psoriasis patients an additional way to manage a complex disease. Preliminary research has shown cannabis to be a promising treatment option for psoriasis and can treat the disease in ways that established first-line therapies currently do not. One of the main hopes for medical cannabis treatment of psoriasis is longer lasting remission from psoriasis symptoms, and research has shown pathways for both topical and systemic treatments to achieve this. This section will examine that research and demonstrate the possible benefits Minnesota patients with psoriasis could experience with medical cannabis treatment.

Psoriasis is a well-researched, yet still not completely understood condition. One well-known pathway that plays a role in psoriasis is the TNF-alpha pathway.[10] Common treatments for psoriasis inhibit this pathway, providing temporary relief from plaques, but no long-lasting relief. Cannabis is a vagal nerve stimulant, and has the ability to therefore modulate the cholinergic anti-inflammatory pathway, which can, in turn, inhibit TNF-alpha, leading to symptom reduction.[11] This is the main proposed pathway through which cannabis could inhibit psoriasis on a systemic level. Of note, this pathway would likely be most effective if treated with systemic cannabis, rather than a topical treatment.

One study of note described how cannabinoids inhibit human keratinocyte proliferation. Human keratinocyte cells contain CB1 and CB2 receptors, which CBD and THC primarily interact with, and hyperproliferation of these cells are what causes psoriasis.[12] Interestingly, this study showed that while cannabinoids do inhibit keratinocyte proliferation, they appear to do through a mechanism other than the CB1/CB2 pathway. When CB1/CB2 antagonists were applied, there was no significant difference in proliferation. Researchers hypothesized the involvement of PPAR-gamma, a different CB receptor which may be implicated in the treatment of various epidermal disorders, including psoriasis.[12] A different recent study also came to the same conclusions, finding that cannabinoid receptors could improve skin barrier condition in the murine psoriasis model.[13] These researchers found that after treating murine models with psoriasis symptoms with a CB1 agonist, inflammation and skin barrier function were improved after three days.[13]

A related set of findings were found in a study by Pucci et. al, titled "Epigenetic control of skin differentiation genes by phytocannabinoids".[14] The authors of the study acknowledge that the endocannabinoid system does play a role in skin cell differentiation, and undertook this

study to investigate if phytocannabinoids—cannabinoids derived from plants such as cannabis—could potentially impact skin physiology in a similar way. [14] This study had a number of interesting findings, the most pertinent being that cannabidiol, an active ingredient in medical cannabis, reduced expression of the skin differentiation gene keratin 10 through a CB1 mechanism. Regarding phytocannabinoids, they conclude "they (especially cannabidiol) have the potential to be lead compounds for the development of novel therapeutics for skin diseases". [14] Of note, this study did not examine THC's involvement in skin cell differentiation, only phytocannabinoids that did not have any psychoactive side effects.

Psoriasis is an inflammatory condition. Discomfort from psoriasis, particularly in psoriatic arthritis, is caused by the inflammation associated with psoriasis. This pain can be debilitating. Fortunately, cannabis is already an established treatment for pain and can be used to reduce inflammation. Thousands of Minnesotans living with intractable pain have had their quality of life improved and pain reduced thanks to medical cannabis, and the same benefits will apply to patients with psoriasis. Psoriasis can also cause a great deal of pruritis, which can significantly impact quality of life. Fortunately, there is evidence that medical cannabis could aid with pruritis, as well. Medical literature has cited the endocannabinoid system, specifically the CB1 Receptor, as a way to reduce itch peripherally and suppress histamine-induced pruritis.[15] The hope is that cannabis will reduce the amount of psoriasis plaques, but even if a patient does not experience improvement with their skin, the hope is that they would at least feel more comfortable, with less pain, itch, and swelling from their psoriasis.

Admittedly, there is not a large amount of research examining the interactions between cannabis and psoriasis, but the above studies examining the endocannabinoid system and how it interacts with keratinocytes and skin cell differentiation show there is potential for cannabis as a treatment option for psoriasis. [16] There are, to the best of our knowledge, no studies that investigate the interaction between cannabinoids and psoriasis in a human model. If psoriasis was added as a certifiable condition, novel research could be undertaken by the state to observe the efficacy of cannabis as a treatment for psoriasis. It would be a unique opportunity for the state to undertake research that has not happened anywhere else. We know from almost one year of manufacturing topical medical cannabis that we can produce a safe and effective topical medication. Minnesota would be the second state in the nation to make psoriasis a qualifying condition, after Connecticut. [17] Promising preliminary research, established safety, combined with anecdotal evidence from current patients who have psoriasis in addition to their qualifying condition, is a solid foundation on which the Minnesotan medical cannabis program can build.

Section F

A selection of studies cited in this petition have been attached.

References

1. National Psoriasis Foundation. Patient Navigation Center: Psoriasis. https://www.psoriasis.org/sites/default/files/psoriasis_fact_sheet_0.pdf. Accessed June 1, 2018.

2. Feldman SR, Tian H, Gilloteau I, Mollon P, Shu M. Economic burden of comorbidities in psoriasis patients in the United States: results from a retrospective U.S. database. BMC Health Services Research. 2017;17(1). doi:10.1186/s12913-017-2278-0.

3. American Academy of Dermatology Association. What is Psoriasis? https://www.aad.org/public/diseases/scaly-skin/psoriasis/what-is-psoriasis. Accessed June 23, 2018.

4. Augustin M, Radtke MA. Quality of life in psoriasis. Handbook of Psoriasis and Psoriatic Arthritis. 2016:101-116. doi:10.1007/978-3-319-18227-8_7.

6. National Psoriasis Foundation. Fact Sheet on Comorbidites. https://www.psoriasis.org/sites/default/files/comorbidities_fact_sheet.pdf. Accessed June 2, 2018.

7. National Psoriasis Foundation. Treatment Comparison. https://www.psoriasis.org/sites/default/files/treatment_comparison_chart_2018.pdf. Accessed June 13, 2018.

8. National Psoriasis Foundation. Fact Sheet on Biosimilars. https://www.psoriasis.org/sites/default/files/biosimilars_fact_sheet_1.pdf. Accessed June 1, 2018.

9. Latest Humira Price Increase Could Add $1 Billion to US Healthcare System in 2018. (n.d.). Retrieved from https://www.centerforbiosimilars.com/news/latest-humira-price-increase-could-add-1-billion-to-us-healthcare-system-in-2018.

10. National Psoriasis Foundation. Patient Navigation Center: Phototherapy. https://www.psoriasis.org/sites/default/files/phototherapy_fact_sheet_0.pdf. Accessed May 30, 2018.

11. Derakhshan N, Kazemi M. Cannabis for Refractory Psoriasis—High Hopes for a Novel Treatment and a Literature Review. *Current Clinical Pharmacology*. 2016;11(2):146-147. doi:10.212174/1574884711666160511150126.

12. Wilkinson JD, Williamson EM. Cannabinoids inhibit human keratinocyte proliferation through a non-CB1/CB2 mechanism and have a potential therapeutic value in the treatment of

psoriasis. *Journal of Dermatological Science*. 2007;45(2):87-92. doi:10.1016/j.jdermsci.2006.10.009.

13. Cannabinoid receptors: Their impact in epidermal differentiation and possible role in treatment of psoriasis. (2015). *Journal of the American Academy of Dermatology,72*(5). doi:10.1016/j.jaad.2015.02.126

14. Pucci M, Rapino C, Francesco AD, Dainese E, Daddario C, Maccarrone M. Epigenetic control of skin differentiation genes by phytocannabinoids. *British Journal of Pharmacology*. 2013;170(3):581-591. doi:10.1111/bph.12309.

15. Chuquilin M, Alghalith Y, Fernandez KH. Neurocutaneous disease: Cutaneous neuroanatomy and mechanisms of itch and pain. *J Am Acad Dermatol*. 2016;74(2):197–212. doi: 10.1016/j.jaad.2015.04.060.

16. Liszewski W, Farah RS. Response to: "The role of cannabinoids in dermatology." *Journal of the American Academy of Dermatology*. 2017;77(3). doi:10.1016/j.jaad.2017.05.023.

17. Dhadwal G, Kirchhof MG. The Risks and Benefits of Cannabis in the Dermatology Clinic. *Journal of Cutaneous Medicine and Surgery*. 2017;22(2):194-199. doi:10.1177/1203475417738971.