From: noreply@pharmacy.ohio.gov
To: MedicalMarijuana@med.ohio.gov
Subject: Condition Petition for Dr James Michael Weeks
Date: Tuesday, December 31, 2019 12:21:41 PM
Attachments: QUESTION 1 pdf version.pdf
QUESTION 2 pdf version.pdf
QUESTION 3 pdf version.pdf
QUESTION 4 pdf version.pdf
QUESTION 5 pdf version.pdf

This message was sent from the Condition page on medicalmarijuana.ohio.gov.

Name: Dr James Michael Weeks
Address: 455 Delta Ave Suite 303, Cincinnati, OH, 45226
Phone: (513) 321-1242
Email: oneheartmedical@gmail.com

Specific Disease or Condition:
CACHEXIA/WASTING SYNDROME

Information from experts who specialize in the disease or condition.
See attached file.

- QUESTION 1 pdf version.pdf

Relevant medical or scientific evidence pertaining to the disease or condition.
See attached file.

- QUESTION 2 pdf version.pdf

Consideration of whether conventional medical therapies are insufficient to treat or alleviate the disease or condition.
See attached file.

- QUESTION 3 pdf version.pdf

Evidence supporting the use of medical marijuana to treat or alleviate the disease or condition, including journal articles, peer-reviewed studies, and other types of medical or scientific documentation.
See attached file.

- QUESTION 4 pdf version.pdf

Letters of support provided by physicians with knowledge of the disease or condition. This may include a letter provided by the physician treating the petitioner, if applicable.
See attached file.

- QUESTION 5 pdf version.pdf

Cachexia/wasting syndrome is a serious but under recognized consequence of many chronic diseases and infections. It is formally defined as a complex metabolic syndrome characterized by loss of muscle with or without loss of fat mass (1). The prominent clinical feature is weight loss, historically defined by total involuntary weight loss of more than 5-10% of pre morbid body weight. However, the measurement of body weight alone may underestimate the frequency of cachexia in patients who are overweight/obese or who have gained weight because of edema or a growing tumor mass. It cannot be reversed with nutritional supplementation alone (2).

The most obvious changes seen in cachexia are a redistribution of the body's protein content, with preferential depletion of skeletal muscle and an increase in the synthesis of the proteins involved in the response to tissue injury. There is increasing evidence that physiologic, metabolic, and behavioral changes of cachexia are highly regulated by cytokines, which trigger synthesis of acute-phase proteins such as tumor necrosis factor-alpha as well as changes in metabolism that provide substrate and energy. The increase in the rate of protein degradation then limits the ability of hyper-caloric feeding to reverse the depletion of lean mass.

It is associated with changes in taste, nausea, lack of hunger at mealtimes, and lack of food enjoyment.

Cachexia has repeatedly been associated with adverse clinical outcomes and poor overall quality of life. It is best described in the setting of cancer but is also seen in other advanced chronic illnesses including, but not limited to, congestive heart failure, chronic obstructive pulmonary disease (COPD), chronic respiratory failure, end stage liver disease ESLD), rheumatoid arthritis, tuberculosis, as well as chronic kidney disease (CKD) and end-stage renal disease (ESRD) (3).

The table below, taken from a 2014 article in the Journal of Cachexia Sarcopenia Muscle, illustrates the clinical impact of cachexia in different common chronic illnesses in Europe.

Table 1 (3)

Estimated clinical impact of cachexia in different chronic illnesses in Europe in 2014. Estimates are assumed to be rather conservative

	Prevalence of illness in population (%)	Patients at risk (%)	Prevalence in patients at risk (%)	Absolute number of patients with cachexia	1-year mortality of patients with cachexia (%)
COPD, moderate	3.5	15	35	1.4 m	15–25
Chronic HF, NYHA II–IV	2.0	80	10	1.2 m	20–40
Cancer, all types	0.5	90	30	1.0 m	20–60
Rheumatoid arthritis, severe	0.8	20	10	120,000	5
End-stage chronic kidney disease	0.1	50	50	185,000	20

aAssumptions are based on a total population of 742 million in Europe. By comparison, the assumed population of the US is 300 million, and of Japan 100 million

The overall prevalence of cachexia is growing in the USA and currently affects around 1% of the patient population, thus around 9 million people. It is also a significant health problem in other parts of the world as well. The prevalence of cachexia varies according to disease, ranging from 5-20% in chronic heart failure to 60% in COPD and as high as 85% in advanced cancer. It is also highly prevalent in moderate to advanced stages of CKD, where loss of weight affects between 18-75% of patients with CKD, with the prevalence depending in part on certain characteristics including requirement for maintenance hemodialysis and presence of co morbid conditions such as heart failure, diabetes mellitus, or liver disease. Hemodialysis patients with anorexia/cachexia have increased risk of hospitalization, poor quality of life, and increased mortality (4).

Cachexia is associated with a poor prognosis overall, with increased morbidity and mortality. In a National Hospice study of terminal cancer, the symptoms of anorexia, weight loss, xerostomia, and dysphagia were all predictive of decreased survival. In addition to cancer, cachexia in the setting of other illnesses, such as heart failure, CKD, HIV, or COPD, has also been shown to increase risk of death. Mortality rates range from 10-15% per year in COPD and 20-30% per year in chronic heart failure and chronic kidney disease to 80% in cancer. In addition to its prognostic value, loss of muscle mass is often associated with poor functional status, impaired quality of life, and an increased risk of hospitalization.

Currently there is no definitive treatment for cachexia available.

General aspects of care include eating with family at the dinner table, eating small frequent high caloric meals, liquid nutritional supplementation and consultation with a nutritionist. In addition, it is important to optimize management of contributing factors including chronic nausea, constipation, taste alterations, dyspnea, and depression.

Despite these general aspects of care, cachexia persists and clinicians often then pursue pharmacological treatments that are available to stimulate the appetite.

Several classes of drugs have the capacity to stimulate appetite, including megestrol acetate, glucocorticoids, anabolic steroids, as well as the emerging role of plant based and synthetic cannabinoids.

Physicians often recommend a short trial of megestrol. Among patients with cancer-related anorexia-cachexia, it had modest beneficial effects on appetite and overall weight though had no effect on overall quality of life, lean body mass, or enhanced survival (5). A significant contraindication to megestrol is recently diagnosed or at risk for thromboembolic events, of significant importance given the fact that many patients whom develop cachexia have conditions that are associated with a hyper coagulable state.

A 2013 Cochrane review of megestrol for treatment of anorexia-cachexia syndrome concluded that compared with placebo, megestrol improves appetite and is associated with slight weight gain in cancer, HIV/AIDS, and other underlying pathology. However, edema, thromboembolic phenomena, and deaths were more frequent in the patients treated with megestrol acetate. The authors concluded that use of megestrol increased mortality (5).

Experience does not support the use of megestrol acetate in patients with anorexia and ESRD. In a small, double-blinded, crossover study, megestrol acetate was administered to patients with ESRD and symptoms of anorexia, and it reported no significant increase in albumin or lean body mass but did result in a number of side effects, including headaches, dizziness, confusion, diarrhea, hyperglycemia, thromboembolism, peripheral edema, and adrenal insufficiency (6).

Megestrol use in the setting of cardiac cachexia is also limited given side effects of peripheral edema and worsening heart failure.

Another treatment option is glucocorticoids. The data to support its use is in cancer patients with anorexia-cachexia syndrome, and there is no evidence for the use of these agents in anorexia-cachexia due to end-stage nonmalignant conditions (7). Side effects include, but are not limited to, immune suppression, myopathy, hyperglycemia, osteoporosis, cataracts, psychosis, adrenal insufficiency.

Anabolic steroids such as testosterone have limited data to support use. Side effects include peripheral edema, abnormal LFT's, depression, as well as virilization in females.

Dronabinol, a synthetic version of the natural phytocannabinoid delta-9-tetrahydrocannabinol (THC), is a drug approved for treatment of cachexia anorexia syndrome in patient with AIDS as well as chemotherapy-induced nausea and vomiting. Dronabinol has can have side effects, which are often dose related. These include dizziness, confusion, worsening psychosis. This synthetic version of THC, with active metabolite 11-hydroxy-delta-9-tetrahydrocannabinol (11-OH-THC) ,been reported to be up to 7 times as potent as natural phytocannabinoid delta-9-THC.

The use of cannabinoids for treatment of appetite loss and cachexia have become a significant focus of interest. 22 states have cachexia listed as a qualifying condition for medical cannabis. These states include Alaska, Arizona, California, Colorado, Connecticut, Delaware, Hawaii, Illinois, Iowa, Louisiana, Maine, Maryland, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Mexico, Oregon, Rhode Island, Vermont and Washington.

Therapeutic cannabis is being more widely used by patents to manage multiple symptoms. A 2017 review of patients seen at a rural academic palliative care clinic in New Hampshire revealed that 27% reported use of cannabis. Some of the most common reasons for use included pain (59%), anorexia (19%), and nausea (16%). This data suggests that a significant minority of patients in a palliative care clinic use cannabis, often for anorexia and nausea (9).

In 2015, “Neuroscience: A cellular basis for the munchies” was published. They studied how and where cannabinoids act in the brain to stimulate appetite. Their research found that POMC neurons (in the hypothalamus) are dense in cannabinoid 1 receptors. When activated by cannabinoids, they stimulate the release of appetite stimulating neuropeptide called beta-endorphin, while somehow avoiding the release of a-MSH (appetite suppressant) (10).

Another study was performed to assess the effects of dosage-controlled cannabis capsules on stimulating appetite in cancer cachexic patients with an end goal of weight gain ≥10%. Patients received 20mg of a 4:1 THC to CBD capsule daily for 6 months. 27% of the patients met the end goal and 27 % had stable weights. Quality of life was also measured, and all reported less appetite loss, improvement in mood, as well as a reduction in pain and fatigue. Tumor necrosis factor levels decreased after cannabis treatment but without statistical significance (11).

Another study performed on 55 patients with a variety of neoplasms suffering from severe nausea or emesis from anti tumor drugs. Each received one of the following antiemetic prophylaxis; THC, prochlorperazine or placebo. Analysis revealed that nausea was absent in 40 out of 55 patients receiving THC, 8 out of 55 receiving

prochloroperizine and 5 out of the 55 in the placebo group. THC appeared to be more efficacious in controlling the nausea and emesis than prochloroperzine or placebo (12).

Reports suggest almost 50% of heart failure patients reported nausea and anorexia in their last 6 months of life. Antiemetics should be considered though conventional treatments including ondansetron, promethazine, prochlorperazine all have the potential of prolongation of the QT interval. QT prolongation can lead to arrhythmias including lethal varieties such as ventricular tachycardia and ventricular fibrillation.

Given the limited efficacy and extensive side effect profile of current conventional therapies for cachexia, we suggest addition of Cachexia/Wasting Syndrome as a qualifying condition for medical cannabis in the state of Ohio. Although current qualifying diagnosis cancer is often associated with cachexia, the addition of cachexia/wasting syndrome will allow an additional subset of patients with advanced respiratory, renal, liver and cardiac diseases access to medical cannabis.

To whom it may concern,

My name is Dr James Weeks. I am a practicing Internist, working both in the inpatient and outpatient setting. I have 10+ years of experience in the field of Internal Medicine and have first had experience in regards to cachexia/wasting syndrome.

I am submitting a proposal to add Cachexia/Wasting syndrome as a qualifying condition for medical cannabis in Ohio.

Please feel free to call me if you have any questions!

Kind regards,

Dr James Weeks
Board certified in Internal Medicine
513-321-1242