MODERN HEALTH CONCEPTS.

Medical Cannabis

THIS INFORMATION IS PROVIDED FOR THE USE OF PHYSICIANS ONLY. THIS INFORMATION IS INTENDED FOR PHYSICIANS TO USE AS A BASIS FOR DETERMINING WHETHER OR NOT TO RECOMMEND MEDICAL CANNABIS TO A PATIENT. THIS MEDICAL AND SCIENTIFIC INFORMATION IS NOT INTENDED FOR USE BY CONSUMERS AND SHOULD NOT BE DISSEMINATED TO CONSUMERS. THE MEDICAL CANNABIS PRODUCTS OFFERED BY MODERN HEALTH CONCEPTS ARE NOT INTENDED FOR USE BY CONSUMERS TO CURE, PREVENT, DIAGNOSE, OR MITIGATE ANY DISEASE OR MEDICAL CONDITION. THIS PRODUCT HAS NOT BEEN ANALYZED OR APPROVED BY THE FDA.

Product Description

Modern Health Concepts produces multiple formulations of medical cannabis using different ratios of CBD:THC to take advantage of the synergistic relationship of cannabinoids.

1:10 CBD:THC

The 1:10 medical cannabis formulation is a THC dominant ratio recommended for qualified patients who respond to the therapeutic actions of THC for their condition.

1:1 CBD:THC

The balanced 1:1 formulation is recommended for qualified patients who respond to the therapeutic actions of both THC and CBD. This ratio may reduce the psychoactive effects of THC.

Medical Cannabis Oil
Ingredients: Natural Medical Cannabis Oil, Non-GMO Safflower Oil

Medical Cannabis Capsules
Ingredients: Natural Medical Cannabis Oil, Non-GMO Coconut Oil, Gelatin Capsule

Medical Cannabis Vaporizer Pen Oil
Ingredients: Natural Medical Cannabis Oil, MCT Oil, Terpenes

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Product Availability:

1:10 CBD:THC

Concentration	OIL			CAPSULE				VAPORIZER PEN
	10 mg THC/mL	10 mg THC/mL	10 mg THC/mL	2mg capsule	5 mg capsule	5 mg capsule	10 mg capsule	300 mg cartridge
Package Size	15 mL	30 mL	60 mL	30 count	15 count	30 count	30 count	1 cartridge
Total THC (per unit)	150 mg	300 mg	600 mg	60 mg	75 mg	150 mg	300 mg	**300 mg**
Price (per unit)	$26.17	$52.34	$92.52	$10.28	$13.08	$26.17	$52.34	$46.73
Price (per mg of THC)	$0.17		$0.15	$0.17				$0.16

1:1 CBD:THC

Concentration	OIL			CAPSULE				VAPORIZER PEN
	10 mg THC/mL	10 mg THC/mL	10 mg THC/mL	2mg capsule	5 mg capsule	5 mg capsule	10 mg capsule	300 mg cartridge
Package Size	15 mL	30 mL	60 mL	30 count	15 count	30 count	30 count	1 cartridge
Total THC (per unit)	150 mg	300 mg	600 mg	60 mg	75 mg	150 mg	300 mg	**150 mg**
Total Active (per unit)	300 mg	600 mg	1200 mg	120 mg	150 mg	300 mg	600 mg	300mg
Price (per unit)	$26.17	$52.34	$92.52	$10.28	$13.08	$26.17	$52.34	$46.73
Price (per mg of Active)	$0.09		$0.08	$0.09				$0.16

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Dosage and Administration Guidelines:

THC Dosing Recommendations:

Due to a wide range of strains and cannabinoid ratios used in clinical studies, usually allowing dosage titration to effect, standard dosage recommendations are difficult to establish.
Primarily because cannabinoid receptors are not located in the brainstem areas controlling respiration, a lethal overdose from cannabis has not been documented. The active dose is very far below any potential lethal dose. However, a narrow index may exist between desired medical benefit and undesirable adverse effects.

A maximum dose will depend on various factors including but not limited to: cannabis experience, tolerance, comorbidities, adverse effects, drug interactions, inter-patient pharmacokinetic variability, and strain and cannabinoid ratios.

Physicians should work closely with patients to determine the dosage that works best for each individual. Starting doses should be small and titration should proceed slowly to prevent or minimize undesirable adverse effects.

Oral Cannabis Pharmacokinetics

Mode of Administration	Time of Onset of Effects	Time of Peak Effects	Duration of Effect
Oral Administration	90 – 120 minutes	2 – 6 hours	4 – 12 hours

Oral Dosing Recommendations

Cannabis Experience	Initial THC Dose	Note	Titration
Cannabis *naïve* patients	2 mg PER DOSE*	Starting with nighttime dosing would be prudent to allow any sedative effects to occur during the night while the patient learns to recognize the effects.	Doses may be titrated upward **slowly** based on effectiveness and observation of any potential side effects. **Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.**
Cannabis *experienced* patients	5 mg PER DOSE*		Doses may be titrated upward **slowly** based on effectiveness and observation of any

			potential side effects. **Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.**

Initial dosing recommendations were established based on the potential for side effects and the importance of **starting low and going slow.*

**ORAL dosing frequency: Re-dosing of orally administered cannabis should be based on the fact that individuals who ingest cannabis may not begin to experience psychoactive or physiological effects for 120 minutes after ingestion. Due to this delay in onset, close observation of any potential side effects is recommended prior to re-dosing. Oral cannabis could potentially be administered between 1-3 times per day.*

Vaporized Cannabis Pharmacokinetics

Mode of Administration	Time of Onset of Effects	Time of Peak Effects	Duration of Effect
Inhalation Administration	90 seconds	15 – 30 minutes	2 – 3 hours

Vaporizer Dosing Recommendations

Each vaporized inhalation delivers approximately **1 mg of Total Active Cannabinoid***

For CBD:THC Ratio 1:1, each inhalation = 0.5 mg THC and 0.5 mg CBD

For CBD:THC Ratio 1:10, each inhalation = 1 mg THC and 0.1 mg CBD

***Multiple variables can potentially affect the amount of mg delivered per inhalation. These variables include battery charge and strength and length of inhalation. This is a limitation with vaporization pen delivery systems, and we recommend patients to recharge their batteries after every 20 inhalations. We recommend that the patient be instructed to inhale for three seconds with button-activated batteries, hold vapor for five seconds, exhale, and then repeat it again at 90 seconds.*

Cannabis Experience	Initial THC Dose	Note	Titration
Cannabis *naïve* patients	1 mg PER DOSE* *For CBD:THC Ratio 1:1 = 2 inhalations; For CBD:THC Ratio 1:10 = 1 inhalation*	Starting with nighttime dosing would be prudent to allow any sedative effects to occur during the night while the	**Inhalations per dose** may be titrated upward **slowly** based on effectiveness and observation of any potential side

		patient learns to recognize the effects.	effects. **Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.**
Cannabis *experienced* patients	2 mg PER DOSE* *For CBD:THC Ratio 1:1 = 4 inhalations; For CBD:THC Ratio 1:10 = 2 inhalations*		**Inhalations per dose** may be titrated upward **slowly** based on effectiveness and observation of any potential side effects. **Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.**

Initial dosing *recommendations were established based on the potential for side effects and the importance of* ***starting low and going slow****.*

VAPORIZER dosing frequency: *Due to the fast onset of action and shorter duration of effects (compared to the oral route of administration), vaporized cannabis may be administered up to* ***4-6 times per day****. However, close observation of any potential side effects is recommended prior to increasing the number of inhalations per dose and the frequency of dosing.*

Qualifying Conditions for Medical Cannabis

If no other satisfactory alternative treatment options exist, and the physician complies with Section 381.986, FS, it may be used for a patient with:

1. A terminal condition as defined under the Florida Statute 499.0295 **Right to Try Act** is a progressive disease or medical or surgical condition that causes significant functional impairment, is not considered by a treating physician to be reversible even with the administration of available treatment options currently approved by the United States Food and Drug Administration, and, without the administration of life-sustaining procedures, will result in death within 1 year after diagnosis if the condition runs its normal course.
2. Any of the following conditions as determined by a licensed Florida physician: cancer, epilepsy, glaucoma, HIV, AIDS, PTSD, ALS, Crohn's disease, Parkinson's disease, multiple sclerosis, or other debilitating medical conditions of the same kind or class as or comparable to those enumerated, and for

which a physician believes that the medical use of marijuana would likely outweigh the potential health risks for a patient, as implemented by Florida Law under Amendment 2. *

**Amendment 2, and the expanded qualifying medical conditions, became effective on January 3, 2017. Section 381.986 F.S. remains in effect and the Florida Department of Health, physicians, dispensing organizations, and patients remain bound by existing law and rule. The Department is committed to quickly moving through the rulemaking process to create a regulatory structure for Amendment 2.*

Pharmacology

The human body has an endogenous cannabinoid (endocannabinoid) system composed of two G-protein coupled receptors (CB1 and CB2), two ligands (anandamide and 2-arachidonylglycerol (2-AG)) and several regulatory enzymes. Most of the biological properties attributed to phytocannabinoids are dependent on their interactions with the endocannabinoid system in humans. There is evidence the endocannabinoid system modulates or regulates various types of physiological processes.

Phytocannabinoids are naturally occurring chemical compounds found within the flowers of the cannabis plant. Currently, more than 100 different phytocannabinoids have been discovered, but only a few of the major ones have been characterized in depth, primarily delta-9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD).

Δ9-THC is one of the most studied and important cannabinoids in the cannabis plant, and is responsible for many effects in animals and humans. THC is a partial agonist of both CB1 and CB2 receptors, but has higher affinity for the CB1 receptor. In addition to being present in the central nervous system and throughout the brain (and likely responsible for the psychoactive effects of THC), CB1 receptors are also found in the immune cells and the gastrointestinal, reproductive, adrenal, heart, lung and bladder tissues, where cannabinoids can also exert their activities. CB2 receptors are primarily found in the immune system and are thought to have immunomodulatory effects and to regulate cytokine activity.

Cannabidiol (CBD) is the major non-psychotropic cannabinoid found in cannabis. CBD exhibits many pharmacological properties and has been shown in vitro and in animal studies to possess anti-anxiety, anti-nausea, anti-arthritic, anti-epileptic, anti-psychotic, anti-inflammatory, neuroprotective and immunomodulatory properties. It has also shown potential as a therapeutic agent in preclinical models of central nervous system diseases such as epilepsy, neurodegenerative diseases, schizophrenia, multiple sclerosis, affective disorders and the central modulation of feeding behavior. CBD appears to reduce the psychoactivity and perhaps other side effects of THC.

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General Dosing Considerations

The pharmacologic effects of medical cannabis are dose-related and pharmacokinetic inter-patient variability should be taken into consideration. The individualization of dose is crucial in the achievement of maximum benefit.

Drug Interactions

Few data are available regarding the potential drug interactions associated with cannabis. Nevertheless, predictions of potential interactions based on the known pharmacology of THC and CBD and the Cytochrome P450 Enzymes can be made.

Any combination with potential for interaction should be used with caution (i.e., conservative dosing, monitoring). This would be especially important with those drugs with a narrow therapeutic index and/or potentially serious dose-dependent side effects (i.e., chemotherapy, cardiac medications, anticonvulsants, etc.). Physicians should coordinate with other medical professionals involved in the patient's care.

In addition, pharmacodynamic interactions should be expected between cannabis and drugs with sympathomimetic activity (tachycardia, hypertension), central nervous system depressants (drowsiness, ataxia), and drugs with anticholinergic effects (tachycardia, drowsiness).

- Alcohol (Ethyl): CNS Depressants may enhance the CNS depressant effect of Alcohol (Ethyl). Monitor therapy.
- Anticoagulants: THC and CBD may enhance the effects of anticoagulants (i.e. warfarin) and therefore may increase levels of INR. Monitor therapy.
- Anticholinergic Agents: May enhance the tachycardic effect of Cannabinoids. Monitor therapy.
- CNS Depressants: May enhance the adverse/toxic effect of other CNS Depressants. Monitor therapy.
- Benzodiazepines: CBD may increase the concentration of benzodiazepines (i.e. clobazam). Levels must be monitored and dosage adjustments may be warranted.
- Selective Serotonin Reuptake Inhibitors: CNS Depressants may enhance the adverse/toxic effect of Selective Serotonin Reuptake Inhibitors. Specifically, the risk of psychomotor impairment may be enhanced. Monitor therapy.
- Sympathomimetics: Cannabinoids may enhance the tachycardic effect of Sympathomimetics. Monitor therapy.
- Zolpidem: CNS Depressants may enhance the CNS depressant effect of Zolpidem. Consider therapy modification.

Please refer to our Drug Interactions document to reference drugs that may potentially interact with medical cannabis based on their metabolic pathways.

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Adverse Effects

Medical cannabis and its analogues are regarded as having a relatively positive safety profile, with mild adverse events commonly including headache, dry eyes, dry mouth, dizziness, light-headedness, numbness, and cough. Serious adverse effects are rare with cannabis or its constituents. Cannabis has low to moderate dependence potential and the active dose is very far below the lethal dose.

THC has been associated with a number of side effects including anxiety, cholinergic deficits, and immunosuppression. THC can produce psychoactive effects that may not be well tolerated in some patients. Patients who are less experienced with cannabis tend to demonstrate more frequent side effects. Cannabinoids often work best in conjunction with other cannabinoids. For example, CBD can mitigate the psychoactive effects of THC. Increases in plasma cortisol due to administered THC have been demonstrated and increases in heart rate, and both transient hypotension and increased systolic blood pressure have also been recorded.

A recent review found that CBD is non-toxic to non-transformed cells and does not affect appetite or various physiologic or psychologic functions. Additionally, it found that chronic use and doses up to 1,500 mg/day were reportedly well tolerated in humans. However, CBD was found to potentially affect hepatic drug metabolism and possibly decrease fertilization capacity. In a study involving a pure CBD extract, the most common side-effects experienced were somnolence, decreased appetite, diarrhea, fatigue and convulsion.

Pregnancy / Lactation

Medical cannabis should not be used during pregnancy. Information regarding safety and efficacy of medical cannabis in pregnancy and lactation is lacking. In retrospective studies, cannabis had a modest effect on fetal growth.
Medical cannabis is contraindicated in breast feeding. THC crosses the placental barrier and is excreted in breast milk. Men and women of child bearing potential should use contraceptive precautions for the duration of therapy with medical cannabis and for three months after discontinuation of therapy.

Precautions and Contraindications

Precautions: Cannabis has additive CNS depressant effects with alcohol, barbiturates and benzodiazepines. Simultaneous use of these compounds with oral Δ9-THC (the major active ingredient of cannabis) may reduce the performance of psychomotor tests, suggesting that those who use any of these drugs together with medical cannabis could expect the effects to be additive. Precaution should be exercised when driving or operating machinery. Due to the possible disruption in the normative neuromaturational processes that occur during adolescence, chronic cannabinoid exposure during adolescence, but not adulthood, may affect cognition later in life. The American Academy of Pediatrics recognizes exceptions should be made for compassionate use in children with debilitating or life-limiting diseases for whom current therapies are inadequate.

Absolute contraindications: Acute psychosis and other unstable psychiatric conditions; serious hypersensitivity to cannabis, or any component of the medical cannabis formulation.

Relative contraindications: Severe cardiovascular, immunological, liver, or kidney disease, especially in acute illness. Cannabis may exacerbate arrhythmia or a history of arrhythmias. The benefits versus risks of the use of cannabis extracts should be carefully weighed in individuals with psychosocial disorders.

Interchangeability

All Medical Cannabis is not therapeutically equivalent to and therefore not interchangeable with any other Medical Cannabis product approved to be dispensed by the Department of Health in the State of Florida. Caution should be used when switching from one approved dispensary's product to another.

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