Haleigh’s Hope TM: Low-THC 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

Haleigh’s Hope Low-THC Cannabis Oil
Strain Ratio 15:1 CBD:THC
Ingredients: Natural Low-THC Cannabis Oil, Non-GMO Safflower Oil

Haleigh’s Hope Low-THC Cannabis Capsules
Strain Ratio 15:1 CBD:THC
Ingredients: Natural Low-THC Cannabis Oil, Non-GMO Coconut Oil, Gelatin Capsule

Haleigh’s Hope Low-THC Cannabis Vaporizer Pen Oil
Strain Ratio 15:1 CBD:THC
Ingredients: Natural Low-THC Cannabis Oil, Terpenes
Product Availability:

<table>
<thead>
<tr>
<th>Concentration</th>
<th>OIL</th>
<th>CAPSULE</th>
<th>VAPORIZER PEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg CBD/mL</td>
<td>20 mg CBD/mL</td>
<td>20 mg CBD/mL</td>
<td>40 mg CBD/mL</td>
</tr>
<tr>
<td>Package Size</td>
<td>15 mL</td>
<td>30 mL</td>
<td>58.5 mL</td>
</tr>
<tr>
<td>Total CBD (per bottle)</td>
<td>300 mg</td>
<td>600 mg</td>
<td>1170 mg</td>
</tr>
<tr>
<td>Price (per bottle)</td>
<td>$51.40</td>
<td>$102.80</td>
<td>$177.57</td>
</tr>
<tr>
<td>Price (per mg of CBD)</td>
<td>$0.17</td>
<td>$0.15</td>
<td>$0.14</td>
</tr>
</tbody>
</table>

Dosage and Administration Guidelines:

**Oral Cannabis Pharmacokinetics**

<table>
<thead>
<tr>
<th>Mode of Administration</th>
<th>Time of Onset of Effects</th>
<th>Time of Peak Effects</th>
<th>Duration of Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Administration</td>
<td>90 – 120 minutes</td>
<td>2 – 6 hours</td>
<td>4 – 12 hours</td>
</tr>
</tbody>
</table>

**Oral Dosage and Administration Guidelines:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Initial CBD Dose</th>
<th>Note</th>
<th>Titration</th>
</tr>
</thead>
</table>
| Chronic Seizures (Cannabis naïve patients) | 0.5 mg/kg/day divided into 3 doses* | 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. | - Initiate with the recommended starting dose and titrate to response. Dose may be increased by 0.5 mg/kg/day increments every 2 weeks.*  
- **Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.**  
- Maximum recommended dose is 6.5 mg/kg/day. The potential for adverse effects increases beyond this dose. |
<table>
<thead>
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</tr>
</thead>
</table>
| Chronic Seizures (Cannabis experienced patients) | 1 mg/kg/day divided into 3 doses*                                                |                                                                                   | - Initiate with the recommended starting dose and titrate to response. Dose may be increased by 0.5 mg/kg/day increments every 2 weeks.*  
- Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.  
- Maximum recommended dose is 6.5 mg/kg/day. The potential for adverse effects increases beyond this dose.                                                                                           |
| Qualifying Condition                          | 10 mg Twice Daily                                                                | 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.                                                    | - Initiate with the recommended starting dose and titrate to response.  
- Amount of mg 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.  
- Maximum recommended dose is 6.5 mg/kg/day. The potential for adverse effects increases beyond this dose.                                                                                           |

*Chronic Seizures*: Dosing will vary depending on patient weight. For capsules, initial dose or incremental titration should be attained by utilizing a combination of 10mg capsules (divided TID) that most closely achieves the total daily dosage recommendations.

*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 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

<table>
<thead>
<tr>
<th>Mode of Administration</th>
<th>Time of Onset of Effects</th>
<th>Time of Peak Effects</th>
<th>Duration of Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation Administration</td>
<td>90 seconds</td>
<td>15 – 30 minutes</td>
<td>2 – 3 hours</td>
</tr>
</tbody>
</table>

Vaporizer Dosing Recommendations

*Each vaporized inhalation delivers approximately 1.5 mg of 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. We recommend that the patient be instructed to inhale for three seconds with button-activated batteries or for five seconds with breath-activated batteries, hold vapor for five seconds, exhale, and then repeat it again at 90 seconds.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Initial CBD Dose</th>
<th>Note</th>
<th>Titration</th>
</tr>
</thead>
</table>
| Chronic Seizures (Cannabis naïve patients) | 0.5 mg/kg/day divided into 3 doses* | 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. | • Initiate with the recommended starting dose and titrate to response. Dose may be increased by 0.5 mg/kg/day increments every 2 weeks.*
  • Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.
  • Maximum recommended dose is 6.5 mg/kg/day. The potential for adverse effects increases beyond this dose. |
| Chronic Seizures (Cannabis Experienced patients) | 1 mg/kg/day divided into 3 doses* | | • Initiate with the recommended starting dose and titrate to response. Dose may be increased by 0.5 mg/kg/day increments every 2 weeks.*
  • Careful monitoring is recommended prior to increasing an individual dose and/or frequency of doses given throughout a day.
  • Maximum recommended dose is 6.5 mg/kg/day. The potential for adverse effects increases beyond this dose. |
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</tr>
</thead>
<tbody>
<tr>
<td>Qualifying Condition</td>
<td>3 Inhalations four times a day</td>
<td>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.</td>
<td>• Initiate with the recommended starting dose and titrate to response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 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.</td>
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<td></td>
<td></td>
<td></td>
<td>• Maximum recommended dose is 6.5 mg/kg/day. The potential for adverse effects increases beyond this dose.</td>
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</table>

*Chronic Seizures:* Dosing will vary depending on patient weight. For the vaporization pen, as each inhalation delivers approximately 1.5 mg, initial dose or incremental titration should be attained by ordering a total amount of mg/day divided 4-6 times per day, as required, that most closely achieves the total daily dosage recommendations.

*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 low-THC Cannabis**

If no other satisfactory alternative treatment options exist, and the physician complies with Section 381.986, FS, it may be used for chronically produced seizures or severe and persistent muscle spasms caused by cancer, cancer-related symptoms, or a physical medical condition.

**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-arthritis, 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.

General Dosing Considerations

The pharmacologic effects of Haleigh's Hope 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. However, caution should be exercised when using doses higher than the maximum recommended dose as the potential for adverse effects increases.

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 Haleigh's Hope based on their metabolic pathways.

### 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.

In a study involving a pure CBD extract, the most common side-effects experienced were somnolence, decreased appetite, diarrhea, fatigue and convulsion. Status epilepticus was a serious adverse event that was possibly related to the product. At higher doses patients taking Haleigh's Hope may experience mild nausea and/or diarrhea. This is thought to be attributed to the larger volume of excipient oil ingested.

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.

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.

**Pregnancy / Lactation**

Haleigh's Hope 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.

Haleigh's Hope 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 Haleigh's Hope 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 Haleigh's Hope (which does contain a very small amount of THC) 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, safflower oil or any component of the Haleigh's Hope 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**

Haleigh's Hope is not therapeutically equivalent to and therefore not interchangeable with any other high-CBD, low-THC 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. This also applies to all non-approved, hemp-grade CBD formulations on the market.
References