



## MÜV™ Evolve Transdermal Gels

500 mg THC

500 mg CBD

250 mg THC and 250 mg CBD (1:1)



POWERED BY  
**müv™**

### Dose

**1 pump delivers 8 mg active dose**

#### THC TOTAL PRODUCT DOSES:

1 bottle contains a total of 500 mg THC and <25 mg CBD, with 60 total doses per bottle

#### CBD TOTAL PRODUCT DOSES:

1 bottle contains a total of 500 mg CBD and <25 mg THC, with 60 total doses per bottle

#### THC/CBD (1:1) TOTAL PRODUCT DOSES:

1 bottle contains a total of 250 mg THC and 250 mg CBD, with 60 total doses per bottle

## MÜV Evolve Encapsulation For Transdermal Cannabis. Localized and systemic relief.

MÜV Evolve Transdermal Gel was designed to more easily penetrate the skin and to target the underlying tissues.



This means that it can be used like any cannabis-infused topical for localized effects of joint inflammation or arthritis discomfort, such as neck, shoulder elbows, and knees. Systemic absorption for full-body effects is accomplished through application to venous regions. Typically, effects are felt within 10-15 minutes and can last 2-4 hours.

\*Patient Information

### Introduction

This pamphlet provides a summary of information about MÜV™ Evolve Transdermal Gels\*. Please read this pamphlet thoroughly and keep it with your medicine. If you have any questions, please consult your physician.

MÜV THC Evolve Transdermal Gel contains 500 mg active ingredient extracted and distilled from *Cannabis* spp. plants meticulously grown without the use of harmful pesticides.

**IMPORTANT: Your physician has recommended this medication for your use only. DO NOT LET ANYONE ELSE USE IT. KEEP THIS MEDICINE OUT OF THE REACH OF CHILDREN AND PETS.**

If a child puts gel on skin or in mouth, remove immediately with towel and soap and water and contact a poison control center. Do not drive a car or operate heavy machinery until you know how this medication affects you. While taking this medication, do not drink alcohol or take other drugs that have an effect on the central nervous system, such as antidepressants or sleep aids.

Unless advised by your physician, do not use this drug if you are pregnant or nursing.

### Clinical Pharmacology

The endocannabinoid system is a series of receptors located throughout the body, which control important biological functions. Your body produces its own endocannabinoids, and cannabinoids like Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) engage these receptors to produce various effects that can promote symptom relief. THC is an agonist of the CB<sub>1</sub> receptor located throughout the central nervous system (CNS) and brain. For this reason, THC is known as the psychoactive cannabinoid, which can produce euphoria or the "high" commonly associated with cannabis use. THC is also a partial agonist of the CB<sub>2</sub> receptor system, so drug interactions with this target should also be considered. Transdermal administration of THC can produce euphoria that accompanies other delivery methods (inhaled, oral, sublingual, etc.), but effects can vary person to person. Typically, transdermal delivery of THC does not produce the same level of euphoria when delivered via other dosing methods. But unlike oral dosing, transdermal delivery negates the hepatic first-pass effect and minimizes the metabolic byproduct, 11-hydroxy THC, which has significantly higher psychoactivity than its predecessor, THC. Because of its unique mode of action, CBD is non-psychoactive and can even reduce the side effects

of THC. When delivered transdermally CBD avoids hepatic-first pass metabolism that is common with oral delivery, which leads to CBD degradation.

The Patented EnCap encapsulation Technology used in this product is a patented encapsulation of cannabis-derived compounds using FDA-approved ingredients that quickens onset time and improves the overall bioavailability of cannabinoids. Common effects of THC include euphoria, relaxation, sedation, increased appetite, and nausea reduction while side effects can include decreased blood pressure, anxiety, or paranoia. Lethal overdose has never been reported with THC or cannabis use.

Due to CB<sub>1</sub> activity in the cerebral cortex, hypothalamus, and other regions of the brain and spinal cord, THC can regulate neurological pain reception. THC has been shown to be effective as conventional opiate treatments for pain reduction and analgesia (Noyes et al. 1975; Maurer et al. 1990; Hosking and Zajicek, 2008). Clinical evidence has also shown THC to be effective in pain management and muscle spasticity/spasms especially in multiple sclerosis (MS) and other chronic pain conditions (Darmani, 2001; De Petrocellis et al. 2000). Inflammation and pain can be alleviated locally or systemically (whole-body) via transdermal application of THC. The anti-inflammatory effects of THC can suppress gastrointestinal symptoms of inflammatory bowel diseases such as Crohn's disease (Naftali et al. 2013). Clinical data has also proven THC to be effective for appetite stimulation in patients with human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS). Additionally, THC acts as an anti-emetic and stimulates appetite for cancer patients undergoing chemotherapy treatments.

Sleep is an important aspect of palliative care and quality of life; and anandamide, a naturally occurring human endocannabinoid, has been shown to illicit sleep responses and improve REM sleep (Murillo-Rodrigueza et al. 1998). Anandamide activates CB<sub>1</sub> receptors, and similarly, THC significantly decreases the time it takes to fall asleep, and once asleep THC led to fewer awakenings during the first half of the night (Cousens and DiMascio, 1973; Nicholson et al. 2004).

There are numerous targets for CBD, but the earliest studies have shown potent neuroprotective properties through antioxidant properties and improvement of certain neurodegenerative disorders (US Patent; Liput et al. 2013). Potent anti-epileptic effects have been demonstrated clinically for particular forms of epilepsy with neuronal protection in the hippocampus (GWPH Trials). Inflammation can be alleviated locally or systemically (whole-body) via transdermal application of CBD (Lodzki et al. 2003).

Due to its interaction with hydroxytryptamine serotonin receptors, CBD has anti-anxiety and anti-depressant effects (de Mello Schier et al. 2014). These indications have also been corroborated with

social anxiety disorders (Bergamaschi et al. 2011) and THC-induced psychosis (Zuardi et al. 1982; Bhattacharyya et al. 2010). The anti-inflammatory effects of CBD coupled with the location of CB<sub>2</sub> receptors in the GI system could provide relief for certain inflammatory bowel diseases (Esposito et al. 2012). The natural terpenes used in MÜV CBD Evolve Transdermal Gel are steam distilled and derived from organically grown plants such as mint and bergamot oil; these essentials oils along with CBD can enhance the entourage effect to promote mental clarity and relieve stress.

Using defined ratios of THC and CBD leads to what is known as the cannabis "entourage effect" which leads to synergistic effects between compounds that would otherwise not be present with single compound treatment. A 1:1 ratio of THC and CBD therefore has both the effects of THC (euphoria, appetite stimulation, pain reduction) as well as CBD (for anxiety, inflammation, and spasticity improvement). Studies have shown that this ratio does not significantly attenuate the effects of THC, suggesting no significant decline in cognitive function (Jacobs et al. 2016). Clinical trials have shown that THC and CBD, co-administered in a 1:1 ratio, demonstrated a marked improvement in sleep quality for conditions ranging from multiple sclerosis, neuropathic pain, intractable cancer pain, and rheumatoid arthritis (Russo et al. 2007). The natural terpenes used in MÜV THC/CBD (1:1) Evolve Transdermal Gel are steam distilled and derived from organically grown plants such as ginger and orange; these essentials oils provide a refreshing scent that can be used throughout the day and enhance the entourage effect of THC and CBD.

## Indications and Use

MÜV Evolve Transdermal Gels can be used for acute conditions from its fast-acting properties due to the Patented EnCap encapsulation. Additionally, the high lipid solubility of the cannabinoids can create a "reservoir effect" in the stratum corneum of the skin (Touitou and Fabin, 1988) and provide longer sustained delivery times of THC and CBD. Conditions for use include: cancer, glaucoma, HIV and AIDS, MS, hepatitis C, amyotrophic lateral sclerosis (ALS), Crohn's disease, Parkinson's disease, or any other debilitating medical condition that a physician believes would outweigh the potential risks for a patient. It can also be used as a palliative care treatment due to its improvements on general outlook including pain, spasticity, weight loss, anxiety, and sleep promotion.

## Dosage and Administration

When starting a new dosing regimen, it is crucially important that medication is administered in small doses (known as titrating) to determine an effective dose and to minimize side

effects. One pump is administered by fully depressing the dispenser on the bottle; one pump contains 500 mg of gel that includes 8 mg active ingredient. It is best to start with one pump at first to know how this product will affect you before increasing the dose.

Common application sites for systemic or full-body effects of MÜV Evolve Transdermal Gel include the inside of the wrist, top of the foot, inner thighs, or the back or sides of the neck. The gel can also be applied to areas of discomfort or inflammation such as joints, hands, or feet for localized symptom relief. Prior to use, clean the application site with soap and water and ensure that the skin is dried and intact before applying the gel. A preferred method for systemic delivery would be to apply the gel directly to the inside of your wrist and rub your wrists together until fully absorbed. Alternatively, dispense the gel onto the affected area and rub in until it is fully absorbed. Try to vary applications sites as this will help achieve more uniform and efficient dosing. Typical onset time for MÜV THC Evolve Transdermal Gel is less than 10 minutes and delivery continues for 2-4 hours. Avoid contact with eyes, nose, and mouth after applying gel and wash hands thoroughly if hands or fingers are used for application.

## Contraindications

Patients known to be allergic to cannabis should not use cannabis products.

Relative contraindications include coronary heart diseases, hypotension, drug abuse, alcohol abuse, mania, depression, bipolar, schizophrenia, or a prior negative reaction to cannabis.

## Warnings and Precautions

**Be sure to notify your physician if you have any of the following:**

- Have or had history of heart disorders because of occasional low blood pressure, high blood pressure, rapid heart rate, palpitations, or fainting;
- Present or past issues with drug abuse;
- Present or past issues with alcohol abuse;
- Have or had mental health problems (depression, mania, bipolar, or schizophrenia);

- Present or past history of epilepsy, seizure disorders, and/or seizure-like activity;
- Have any allergies to drugs;
- Are pregnant or nursing, or intend to become pregnant.

If you become pregnant while taking any MÜV cannabis-infused product, stop using immediately and consult with your physician.

MÜV Evolve Transdermal Gels should be used with caution, particularly with children and elderly patients, as there are few studies in these patient populations. A physician should monitor children under the age of 18 closely as THC can have adverse effects on brain development.

When consulting with your physician, please include all current medications (both prescription and non-prescription) as MÜV Evolve Transdermal Gels can theoretically interact with other drug therapies. Avoid grapefruit or grapefruit juice and other CYP450 inhibitors as these can adversely affect THC treatments. Adverse reactions could also occur with alcohol and other drugs that affect the CNS (such as Valium, Librium, Xanax, Seconal, Nembutal, or Phenobarbital).

## Adverse Reactions

**Tell your physician if any symptoms persist or worsen with time:**

- Cardiovascular: palpitations, tachycardia, vasodilation, hypotension (low blood pressure);
- Digestive: dry mouth, abdominal pain, nausea, vomiting, diarrhea, constipation, anorexia, excessive appetite, hepatic enzyme elevation;
- Nervous System: euphoria, drowsiness, memory loss, confusion, anxiety, paranoia, depersonalization, hallucinations, poor balance, dizziness, somnolence, nightmares, depression, difficulty speaking;
- Musculoskeletal: myalgias;
- Skin: flushing, sweating, irritation at application site;
- Ocular: conjunctivitis, impaired vision, irritation;
- Body: chills, headache, fatigue;
- Respiratory: cough, rhinitis, sinusitis.

**INACTIVE INGREDIENTS (All USP or Pharma-grade):** Purified Water, Ethanol, Oleic Acid, Propylene Glycol, Polysorbate 20, Natural Essential Oils, Triethanolamine, and Carbomer Polymer.

## FAQ

### ***IS IT PSYCHOACTIVE?***

Two of the Thrive Transdermal Gels are psychoactive: MÜV THC & MÜV 1:1.

### ***HOW DOES IT CROSS THE BLOOD-BRAIN BARRIER?***

THC and CBD are fat-soluble, so they can only penetrate the upper levels of the fatty dermis, resulting in localized pain relief. The EnCaps™ encapsulation technology utilizes a water-soluble gel to create a little envelope in which THC and CBD are shuttled to the bloodstream. Once the shuttle hits the bloodstream, the cannabinoids are released, resulting in fast-acting, systemic effects.

### ***WHAT IS THE POTENCY?***

One metered pump of our transdermal gel is 8 mg.

### ***HOW DO I USE IT/WHERE DO I PUT IT?***

Where you put it is dependent on the effects you're seeking. Applying on a thin-skin, high blood flow area allows for maximum bloodstream penetration for full body effects. Applying on your shoulder or back, for example, will provide a deeper, more localized pain relief, as the layers of the dermis are thicker.

### ***WHAT IS IT MOST EFFECTIVE FOR?***

Patients report great effects in terms of pain flare up management and as a sleep aid, as well as for anti-nausea and anti-anxiety effectiveness.

### ***HOW LONG WILL EFFECTS LAST?***

Thrive Transdermal Gel has an onset time of about 10-15 minutes, with a duration of two to four hours.

### ***HOW SHOULD I DECIDE BETWEEN TYPES (CBD, 1:1, THC)?***

The formulation is dependent on the symptoms you are trying to treat.

### ***HOW LONG WILL THIS BOTTLE LAST?***

There are 60 pumps in each bottle of Thrive Transdermal Gel.

### ***WHAT ARE THE NATURAL FRAGRANCE INGREDIENTS IN THRIVE TRANSDERMAL GEL?***

MÜV THC—Ylang Ylang, Lavender and Chamomile

MÜV 1:1—Orange and Ginger

MÜV CBD—Bergamot, Spearmint and Ylang Ylang