CYBIS™ 10:25

Product Information Leaflet

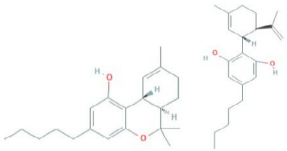
Description

Cybis™ 10:25 oil is a formulated full spectrum medicinal cannabis product. The product is manufactured in Australia under GMP conditions.

Each 1 mL of Cybis™ 10:25 oil contains 10 mg tetrahydrocannabinol and 25 mg cannabidiol as active ingredients. Cybis™ 10:25 oil also contains 1 mg/mL linalool (terpenoid), with medium chain triglyceride (MCT) as a carrier. Tetrahydrocannabinol (THC, also known as δ-9-tetrahydrocannabinol) has a molecular formula $C_{21}H_{30}O_2$, molecular weight of 314.47 g/mol, and CAS Number of 1972-08-03.

Cannabidiol (CBD) has a molecular formula of $C_{21}H_{30}O_2$, molecular weight of 314.5 g/mol and CAS Number of 13956-29-1.

The chemical structures of THC and CBD are shown below.



THC CBD

Dosage and administration

DOSAGE

Adults

It may take several weeks to find the optimum dose and undesirable effects can occur during this time, most commonly dizziness, somnolence or fatigue. These undesirable effects are usually mild and resolve in a few days.

Titration period:

A titration period is required to reach the optimum dose. The optimum dose will vary depending on the patient, the condition being treated and the prescriber.

The dose should be increased each day following the schedule given in the table below or as directed by the prescriber until adequate symptom relief is achieved. If undesirable effects become troublesome the dose should be reduced until the undesirable effects disappear or become tolerable.

Maintenance period:

The optimum dose is the lowest dose that achieves the desired benefit without unacceptable side effects. Following the titration period, patients are advised to maintain the optimum dose achieved. Re-titration upwards or downwards may be required if there are changes in the severity of the patient's condition, changes in their concomitant medication or if troublesome adverse reactions develop.

Children

Cybis™ 10:25 is not recommended for use in children or adolescents below 18 years of age due to lack of safety and efficacy data.

Suggested Cybis™ 10:25 dose

Days	Dose	THC per day	CBD per day
1 to 7	0.5 mL once-daily	5 mg	12.5 mg
8 to 14	0.5 mL twice-daily	10 mg	25 mg
15 to 21	1.0 mL twice-daily	20 mg	50 mg
22 to 28	1.5 mL twice-daily	30 mg	75 mg

Maximum daily dose recommend is 3.0 mL (75 mg CBD + 30 mg THC).

METHOD OF ADMINISTRATION

Cybis™ 10:25 is for oromucosal use only.

In the absence of compatibility studies, Cybis™ 10:25 must not be mixed with other medicinal products.

1. Shake the bottle gently before use.
2. Withdraw the required dose into the syringe.
3. The oil should be placed under the tongue with the syringe.
4. The syringe should be washed and allowed to dry after use.

STEP 1 STEP 2 STEP 3

Presentation and Storage conditions

Cybis™ 10:25 is an opaque/cloudy dark brown liquid containing 10 mg/mL of THC and 25 mg/mL CBD. The product is packaged in an amber glass bottle with child resistant polypropylene (PP) cap with low density polyethylene (LDPE) syringe adapter and polyethylene/polystyrene syringe.

Pack Size: 30 mL

Storage conditions: Store upright in the original container, tightly closed. Store below 25°C. Protect from light and moisture.

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

Indications

Cybis™ 10:25 is indicated for medical conditions as specified by the authorised prescriber through the Therapeutic Goods Administration Special Access Scheme (Category B).

Cybis™ 10:25 is not registered on the Australian Register of Therapeutic Goods and as such no specific indications have been approved for the product. The product is only available through the Special Access Scheme or an approved clinical trial.

Contraindications

Cybis™ 10:25 is contraindicated for use in patients:

- With hypersensitivity to cannabinoids or to any of the excipients in the product.
- Who are pregnant or breastfeeding.
- With an active psychotic or mood or anxiety disorder, or previous history of psychotic disorder.
- With unstable cardiovascular disease.

Precautions

Particular caution should be taken with the use of Cybis™ 10:25 in patients:

- With a history of substance abuse.
- With moderate to severe renal or hepatic impairment.
- With weakness and wasting of the body due to severe chronic illness.
- With neurological conditions, who may be more likely to experience adverse effects.
- Aged 65 years and over, who may be more likely to experience adverse events.

Patients should not drive or operate heavy machinery while being treated with Cybis™ 10:25.

Drug interactions

There is limited information on how Cybis™ 10:25 may interact with other prescription, over-the-counter and herbal medicines. The following interactions may occur:

Drugs metabolised by cytochrome P450:

The main active ingredients of Cybis™ 10:25 are metabolised by cytochrome P450. If Cybis™ 10:25 is administered with other drugs metabolised by cytochrome P450 enzymes such as **clobazam** a decrease in efficacy or increase in adverse effects from either drug may be noted.

Drugs that inhibit or induce cytochrome P450:

If administration of drugs that inhibit cytochrome P450 (such as **ketoconazole, itraconazole, ritonavir, clarithromycin, fluoxetine**) or that induce cytochrome P450 (such as **rifampicin, carbamazepine, phenytoin, phenobarbital, St John's Wort**) is commenced or ceased during treatment with Cybis™ 10:25, re-titration of Cybis™ 10:25 may be required.

Analgesics or sedatives, including alcohol:

Administration of Cybis™ 10:25 with analgesics or sedatives such as **benzodiazepines, alcohol, barbiturates, anticholinergics, antiepileptics or antidepressants** may product additive sedative and muscle relaxant effects. Use of alcohol should be avoided during treatment with Cybis™ 10:25.

Highly protein bound drugs:

If Cybis™ 10:25 is administered with other highly protein-bound drugs with narrow therapeutic index (such as **warfarin, cyclosporine, amphotericin B**), patients should be monitored for increased adverse effects as Cybis 10:25 may increase the free fraction of these drugs.

Digoxin:

Cybis™ 10:25 may inhibit p-glycoprotein for which **digoxin** is a substrate. Caution is recommended in concomitant administration of Cybis™ 10:25 and digoxin or other p-glycoprotein substrates.

Adverse reactions

No information specific to Cybis™ 10:25 is available in relation to adverse events. Adverse reactions most commonly associated with medicinal cannabis products include:

- Dizziness or vertigo
- Drowsiness, fatigue,
- Nausea, vomiting, diarrhoea
- Dry mouth
- Thought disturbance,
- Cognitive or attention disturbance
- Increased or decreased appetite

Dizziness and drowsiness may be more common during the initial titration period. The majority of adverse reactions are mild to moderate and may resolve with continued treatment.

The following adverse reactions have been reported with high doses of THC:

Convulsions, feeling high or feeling dissatisfied, depression, confusion, hallucinations, paranoid delusions, psychosis, and cognitive distortion (having thoughts that are not true). These adverse reactions are not expected if Cybis™ 10:25 is administered at recommended doses.

Pharmacology

Mechanism of action

Cannabinoid receptors CB1 and CB2 are the primary receptor subtypes that constitute the endocannabinoid system. CB1 is the most widely-expressed receptor from the G protein family in the brain and is highly expressed in the areas associated with reward, emotional and cognitive processing. CB2 receptors are predominantly found on immune cells and other peripheral tissues including the peripheral nervous system, cardiovascular system, GI tract, liver, adipose tissue, bone and reproductive system.

THC is the main psychoactive component of cannabis. Conversely, CBD is considered non-psychoactive. Furthermore, evidence suggests that CBD attenuates the acute psychoactive effects of THC. CBD acts as a negative allosteric modulator of CB1 receptors – allowing CBD to bind with the receptor and antagonise the action of THC while not inducing any downstream pharmacological effects. Additionally, CBD acts as an agonist of receptors involved in anxiety (5HT1) and fat storage (PPARγ), an antagonist of receptor GPR55 a receptor involved in a range of cannabinoid effects, and an inhibitor of Fatty Acid Amide Hydrolase enzyme which breaks down fatty acid amides including the endogenous cannabinoid anandamide.

Pharmacokinetics

Pharmacokinetic or pharmacodynamic data have not been obtained for Cybis™ 10:25 oromucosal liquid. Pharmacokinetic parameters may vary from patient to patient.

Absorption

After oromucosal administration, both THC and CBD undergo fairly rapid absorption via the oral mucosa appearing in the plasma within 15 minutes of administration. Peak plasma concentrations are reached in approximately 60 minutes. Oromucosal administration avoids first pass metabolism and produces higher plasma drug concentrations relative to oral administration. However, part of the dose may also be swallowed and orally absorbed.

Distribution

Cannabinoids are highly lipophilic and are rapidly distributed into well-vascularised organs including lung, heart, brain, and liver. The volumes of distribution (Vd) are ≈32 L/kg (calculated following intravenous administration) and ≈3.4 L/kg (following inhaled administration) for THC and CBD respectively. Plasma protein binding is high at around 97% for THC and ≈90% for CBD. THC and CBD may also accumulate in adipose tissues from which they are slowly released at sub-therapeutic levels back into the bloodstream.

Metabolism

THC and CBD are predominantly metabolised in the liver, and approximately one third of the parent drugs and their metabolites are subsequently excreted in the urine and faeces. THC is metabolised by cytochrome P450 (CYP450) isozymes CYP2C9, CYP2C19, and CYP3A4. CBD is primarily metabolised by CYP2C19 and CYP3A4, and additionally CYP1A1, CYP1A2, CYP2C9 and CYP2D6.

Excretion

The estimated elimination half-lives of cannabinoids are of the order of 24 to 36 hours or longer. THC may take up to 5 days for 80-90% of the dose to be eliminated in the urine or faeces. CBD has an average terminal elimination half-life following intravenous dosing to be approximately 24-36 hours.

POISONS SCHEDULE

Poisons Schedule:
Schedule 8 CONTROLLED DRUG

Possession without Authority Illegal.

Keep Out of Reach of Children

Available only on prescription through the Special Access Scheme (Category B), by an Authorised Prescriber, or as part of an approved clinical trial.

SPONSOR DETAILS

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