

Canada-Approved Medicine: This monograph describes a medication approved for use in Canada by the Therapeutic Products Directorate, a division of Health Canada's Health Products and Food Branch. The medication is not approved by the United States Food and Drug Administration; however, a similar formulation carrying a different generic or brand name might be available in the U.S.

## cannabidiol (ka-na-bi-dye-ole)

### delta-9–tetrahydrocannabinol (THC)

(del-ta nine tet-re-hye-dro-ka-na-bi-nole)

✳ Sativex

#### Classification

*Therapeutic:* analgesic adjuncts, therapeutic, antispasticity agents

*Pharmacologic:* cannabinoids

#### Indications

Adjunct treatment of spasticity in adults with multiple sclerosis (MS) who have not responded to other therapies. Analgesic adjunct in the management of neuropathic pain in patients with MS or advanced cancer who have not responded to opioids or other analgesics for severe pain.

#### Action

Acts on cannabinoid receptors located in pain pathways in the brain, spinal cord and peripheral nerve terminals. Has analgesic and muscle relaxant properties. **Therapeutic Effects:** Decreased pain and spasticity.

#### Pharmacokinetics

**Absorption:** Buccal absorption is slower than inhalation.

**Distribution:** Highly lipid soluble, distributes and accumulates in fatty tissues. Cannabinoids enter breast milk in considerable amounts.

**Metabolism and Excretion:** Some first-pass hepatic metabolism occurs; highly metabolized by the CYP450 enzyme system. Metabolites can be stored in fatty tissues and re-released over time (up to weeks); one metabolite of THC is pharmacologically active (11–hydroxy-THC). Further metabolism occurs in renal and biliary systems.

✳ = Canadian drug name.

⚡ = Genetic Implication.

CAPITALS indicate life-threatening, underscores indicate most frequent.

~~Strikethrough~~ = Discontinued.

**Half-life:** Bi-exponential half-lives with short initial phases of *Cannabidiol*—1.4–1.8 hr; *THC*—1.3–1.7 hr *11–hydroxy-THC*—1.9–2.1 hr; terminal elimination half-life of *cannabinoids*—24–26 hr or more.

TIME/ACTION PROFILE (analgesic and antispasticity effects)

ROUTE	ONSET	PEAK†	DURATION
cannabidiol	unknown	1.6–2.8 hr	up to 12 hr
THC	unknown	1.6–2.4 hr	up to 12 hr

†Blood levels peak more quickly when administered under the tongue.

#### Contraindications/Precautions

**Contraindicated in:** Allergy/hypersensitivity to cannabinoids, propylene glycol or peppermint oil; Serious cardiovascular disease, including ischemic heart disease, arrhythmias, poorly controlled hypertension or severe heart failure; History of schizophrenia/psychoses; Patients with child-bearing potential who are not using reliable contraception; Sore/inflamed mucosa (may alter absorption); **OB:** Pregnancy (avoid use); **Lactation:** Avoid breast feeding (Cannabinoids enter breast milk in considerable amounts); **Pedi:** Safe and effective use in children <18 yr has not been established; avoid use.

**Use Cautiously in:** History of epilepsy/recurrent seizures; History of substance abuse; Perioperative state (consider possible changes in cardiovascular status); History of depression/suicide attempt or ideation; Significant hepatic/renal impairment; Patients with child-bearing potential (reliable contraception must be ensured); Cancer patients with urinary tract pathology (↑ risk of urinary tract adverse reactions); **Geri:** should used cautiously in this population.

#### Adverse Reactions/Side Effects

**CNS:** dizziness, fatigue, confusion, depression, disorientation, drowsiness, euphoria, hallucinations, psychotic reactions, suicidal ideation, weakness. **CV:** hypertension, palpitations, tachycardia, postural hypotension. **GI:** appetite change, constipation, dry mouth, dysgeusia, mucosal/teeth discoloration, nausea (↑ in cancer patients), stomatitis. **GU:** urinary retention (↑ in cancer patients). **Local:** application site irritation. **Misc:** physical dependence, psychological dependence.

#### Interactions

**Drug-Drug:** some ↑ risk of CNS depression with other CNS depressants including alcohol, some antidepressants, some antihistamines, benzodiazepines, GABA

**inhibitors, sedative/hypnotics, opioids and psychotropics/antipsychotics.** Cannabidiol inhibits the CYP450 enzyme system; may ↑ effects of **amitriptyline, alfentanil, fentanyl and sufentanil.**

**Drug-Natural Products:** ↑ risk of intoxication with other forms of **cannabis.**

### Route/Dosage

**Buccal (Adults): Day 1**—One spray in the morning and one in the evening; *subsequent days*—Increase by one spray/day. Wait at least 15 min between sprays. Spread out sprays used per day. If unacceptable effects occur temporarily discontinue and re-institute at a lower amount sprays/day or longer intervals between sprays. Titrate to optimal maintenance dose (usual range 4–8 sprays/day, usually not more than 12 spray/day; higher doses have been used/tolerated). Adjust dose to changes in patient condition.

## NURSING IMPLICATIONS

### Assessment

- Assess patient's pain level before and after cannabidiol.

### Potential Nursing Diagnoses

Acute pain  
Chronic pain

### Implementation

- Administer one spray 2 times a day, in morning and in evening, on first day. Administer under tongue or in buccal area. Rotate sites in mouth to avoid irritation. Effects should be noticed in about 30 minutes. Do not spray the back of throat or into nose. After first day, increase dose by 1 spray every 24 hours, spacing doses evenly. No more than 12 doses should be used over a 24 hour period. Space each spray by at least 15 min.
- Prime pump before first use. Shake vial gently and remove protective cap. Hold vial in an upright position and press firmly and quickly on the actuator 2 or 3 times, until a fine spray appears. Point spray into a tissue, away from patient.

### Patient/Family Teaching

- Caution patient to use medication as directed.
- Instruct patient on correct spray technique. Instruct patient to rotate sites in the mouth between under the tongue and buccal locations.

- Instruct patient to store unopened bottles in refrigerator. Do not freeze. Keep away from sources of heat such as direct sunlight or flames (product is flammable). Opened bottles may be stored at room temperature. Keep out of reach of children.
- Inform patient that any unused contents should be discarded after 28 days. Do not dispose of medications in wastewater (e.g. down the sink or in the toilet) or in household garbage. Consult pharmacist how to dispose of expired or unneeded medication.
- Caution patient to avoid alcohol while taking cannabidiol.

### Evaluation/Desired Outcomes

- Decrease in pain.
- Decrease in muscle spasticity.

### Why was this drug prescribed for your patient?