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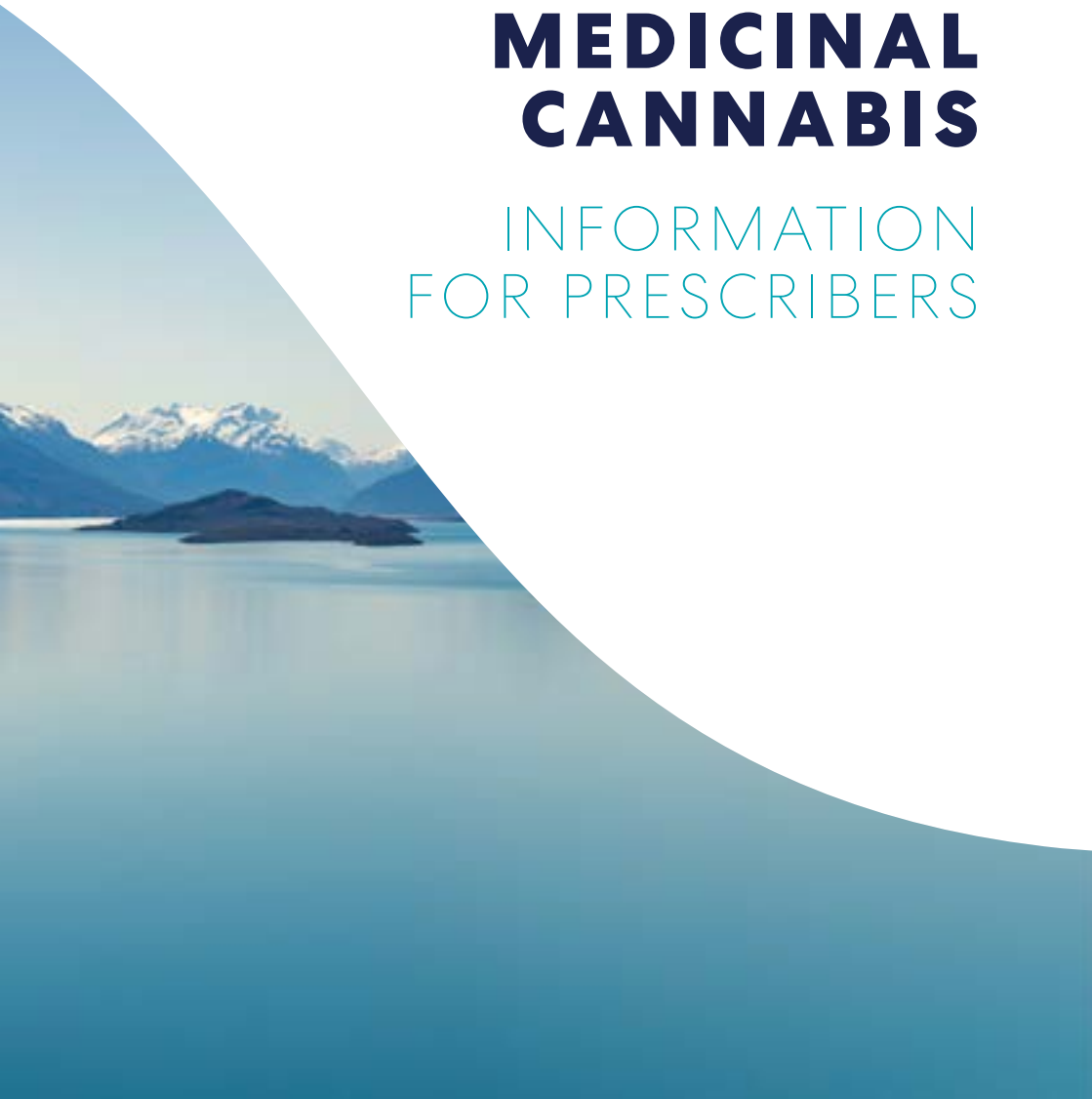
PHARMACEUTICALS

MEDICINAL CANNABIS

INFORMATION FOR PRESCRIBERS



CANNABIS CONSTITUENTS

CANNABINOIDS

Cannabinoids are produced mostly in their inactive forms, in the female cannabis flowers/buds. Heating (at temperatures above 120°C) promotes decarboxylation (activation) of cannabinoids. Two widely studied cannabinoids are tetrahydrocannabinol (THC) and cannabidiol (CBD).[1]

THC has an euphoriant effect, and can also act as[2,3,4,5,6,7]

- Antiemetic
- Analgesic
- Anti-inflammatory
- Anti-pruritic
- Muscle relaxant

CBD does not have intoxicating effects and may be useful in the management of seizures, pain, and may have anxiolytic and antipsychotic effects.[8,9]

Pre-clinical (animal) studies show that the cannabinoid acids (precursors of CBD and THC) might have a therapeutic effect:[1,10]

- CBDA has anti-inflammatory, anti-emetic, anti-convulsant and anti-carcinogenic properties.
- THCA is ten times more potent than THC in reducing acute and anticipatory nausea.

TERPENES

Terpenes are the largest group of phytochemicals and are present in many plants.[11] Cannabis contains up to 200 different terpenes. The terpene profile of a cannabis plant contributes to its scent and flavour and may also influence how each cannabis cultivar impacts each person. Terpenes may have medicinal properties of their own, in addition to working with CBD, THC and other cannabinoids to produce the overall therapeutic effect of a product.[11,12]

INHALATION V ORAL ADMINISTRATION[1,8,13]

	INHALATION	ORAL
Onset	5-10 mins	1-3 hours
Estimated duration effect	2-4 hours	6-8 hours
Absorption	Through lungs, directly into bloodstream	From GI tract, metabolised in the liver before entering bloodstream
Bioavailability	30-50%	10-20%

Cannabis isn't a one-size fits-all therapy. Many patients benefit from using more than one product, for example, a product for medicating during the day and another for the evening, and/or for different symptoms. An informed and ongoing discussion between a patient and their doctor is important to finding the right product and dose.

BEFORE PRESCRIBING[8,14]

CONSIDER

1. Presenting symptoms.
2. Past medical history *(cardiovascular disease, liver disease and renal disease; conventional treatments that have been tried and have failed, as well as the length of time the treatments were trialled and the reasons for ceasing).*
3. Psychological and psychiatric history *(history of mental illness, particularly schizophrenia - including family mental health history).*
4. Risk behaviours associated with drug dependence *(while previous /current cannabis use may not be a contraindication, care should be taken to manage the risk of dependence; nicotine dependence, alcohol dependence/abuse).*
5. Social history *(employment, especially where it involves driving or operating machinery; risk of falls (in older patients or younger patients with mobility concerns); family responsibilities such as caring for young children).*
6. Physical investigations as needed.
7. Medication review *(other medications that might interact with medicinal cannabis; risk of side effects of medicinal cannabis products).*

PRACTICAL CONSIDERATIONS[1,8,15]

- Dosing is highly individualised and relies on titration of the product, regardless of the cannabinoid content, using the principle 'start low and go slow'. Titrate to find the dose where therapeutic effect is maximised, and adverse effects are minimised.
- Increase doses slowly, preferably weekly.
- First dose should be given in the evening to assist with the management of side effects, and patients should be advised to have someone with them should they experience any adverse effects.
- Be mindful of maximum daily dose of THC. Lower doses are less likely to be associated with adverse effects.
- CBD is not problematic in clinical practice. A maximum dose is yet to be established, except in severe epilepsy 25mg/kg/day. The majority of patients are on 100-800mg/day depending on therapeutic use.

PROPOSED TREATMENT PLAN

The medicinal cannabis product should be trialled for one-month, to determine the effectiveness of the medication for the patient's condition/symptoms. The treatment plan should indicate[14]

- Treatment goals - *starting and stopping - documented and discussed with the patient.*
- Risk management processes, *such as frequency of dispensing (e.g. weekly dispensing if there are concerns that patient may self-escalate their dose).*
- Monitoring arrangements - *weekly/fortnightly/monthly reviews, any blood tests, specialist reviews, other investigations (as needed) for the particular medical condition and/or symptoms being treated.*
- Exit strategy - *for situations where the medicinal cannabis product is not helping to manage the symptoms, or the goals of treatment are not reached.*
- Informed consent - *obtained and the patient provided with information about the medicinal cannabis product, possible side effects and treatment goals, and that treatment will be discontinued if benefit has not been demonstrated (the patient should sign and be given a copy of the plan with a copy filed in the patient's medical record).*

STOPPING

Cannabinoids should be ceased where[14]

- The desired effect is not apparent after 4–12 weeks; and
- Intoxicating or other side-effects are prohibitive (particularly for THC preparations).

There is little information on dose-response. Starting doses should be low, and the dose increased in response to lack of efficacy until toxicity outweighs any benefit.

PROPOSED DOSING AND TITRATION PROTOCOLS

OIL FORMULATION

"Start Low, Go Slow" principle[15]

THC maximum daily dose 30 mg/day[16]

This dosing table serves as a guide. The dose may differ based on the prescriber's recommendations	INCREASE ONLY IF NEEDED			
Active ingredient*	Week 1	Week 2	Week 3	Week 4
THC	2.5 mg nocte	5 mg nocte	2.5 mg mane + 5 mg nocte	5 mg mane + 5 mg nocte
CBD#	25 mg mane + 25 mg nocte	50 mg mane + 50 mg nocte	**	**

Treatment-resistant paediatric epilepsy, seek specialist advice - 2 to 5 mg/kg per day divided in twice-daily dosing.

* Products containing both CBD and THC, THC dose should not exceed the maximum dose reccomended.

** Most patients find their CBD dose by week 2. Prescriber might recommend 1 week break if side effects are encountered.

Example 1. Product with CBD 100mg/ml

- Week 1: 0.25 ml mane and 0.25 ml nocte
- Week 2: 0.5 ml mane and 0.5 ml nocte

Example 2. Product with CBD 10mg/ml & THC 10mg/ml

- Week 1: 0.25 ml nocte
- Week 2: 0.5 ml nocte
- Week 3: 0.25 ml mane and 0.5ml nocte
- Week 4: 0.5 ml mane and 0.5ml nocte

DRY FLOWER FORMULATION - INHALATION

It is recommended that patients prescribed dry flower for inhalation start with 1 inhalation, wait 15 minutes, and then increase by 1 inhalation every 30 minutes until clinical effect is reached, and as tolerated, to the max. daily dose[16].

"Suggested 2-3-4 Inhalation Method": inhale for 2 seconds, hold for 3, exhale for 4. Maximum 4 inhalations recommended[17]

Maximum THC daily dose: 5g/day[15], majority of Australian patients take 1-2g/day.

This dosing table serves as a guide. The dose may differ based on the prescriber's recommendations	INCREASE ONLY IF NEEDED		
Active ingredient	Week 1	Week 2	Week 3
THC +/or CBD	0.1-0.2g nocte*	0.1-0.2g mane+ 0.1-0.2g nocte	0.25g mane+ 0.25g nocte

Dry flower formulations that have been prescribed for inhalation by the Prescriber are to be administered via vaporisers registered as medical devices, like the Mighty Medic and Volcano Medic 2. *0.1-0.2g is approximately ½ teaspoon; most patients get good symptom relief from 0.2-0.25g. Vaporisers are not for patients under 18yo, or patients with known respiratory tract and lung conditions.

DRY FLOWER FORMULATION - TEA[18,19]

Heating/activation of cannabinoids takes place through boiling (100°C).

Method of administration:

- Boil 500 ml (0.5 litres) of water in a covered vessel
- Grind product into fine pieces
- Add 0.5 grams of product to vessel
- Simmer (15 mins, lid on)
- Remove from heat, strain tea
- Store the leftover tea in a thermos (same day administration)
- If the patient wishes to make tea for a few days in advance, 1 gram (about 4 teaspoons) of medicinal cannabis should be used per litre of water.

This dosing table serves as a guide. The dose may differ based on the prescriber's recommendations	INCREASE ONLY IF NEEDED
Active ingredient	Week 1	Week 2
THC +/or CBD	1 cup (200ml) nocte	1 cup (200ml) mane+ 1 cup (200ml) nocte

After preparation, the patient should add 1 sachet or teaspoon of coffee creamer powder to warm tea. This prevents the active ingredients in the tea from sticking to the inside of the teapot or mug after cooling, which could reduce the efficacy of the tea.

Example. Product with CBD 125mg/g and THC< 10mg/g

- Week 1: 200 ml (25 mg CBD;< 2 mg THC)
- Week 2: 200 ml (25 mg CBD;< 2 mg THC) mane and 200 ml (25 mg CBD;< 2 mg THC) nocte

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The primary purpose for this educational resource is to support informed decision making and to aid the conversation between the doctor and the patient. As with all therapies, medical practitioners must exercise their professional judgment in determining the appropriate therapy for an individual patient. This educational resource is not a summary of peer-reviewed literature and international reviews concerning potential therapeutic uses and harmful effects of cannabis and cannabinoids. Also, it is not a systematic review or meta-analysis of the literature and has not rigorously evaluated the quality and weight of the available evidence nor has it graded the level of evidence. It is not meant to be comprehensive and should be used as a complement to other reliable sources of information. Despite the similarity of format, it is not a Data Sheet. A Data Sheet is a document which would be required if a product were to receive an approval for distribution in New Zealand. Most cannabis-based products are unapproved therapeutic products in New Zealand, prescribed under section 29 of the Medicines Act 1981.

The provision of this information should not be interpreted as an endorsement of the use of a certain cannabis-based product, or cannabis and cannabinoids generally by NUBU Pharmaceuticals. This educational resource should not be construed as expressing conclusions or opinions from NUBU Pharmaceuticals about the appropriate use of cannabis or cannabinoids for medical purposes. NUBU Pharmaceuticals, Auckland, New Zealand. info@nubupharma.com. 0800 463 3226. Date of preparation March 2022.