

An overview of medicinal cannabis for health practitioners

Recent regulatory changes will make medicinal cannabis much more accessible to patients. As medicinal cannabis is not a focus of conventional medical training, many health professionals are likely to have questions about the risks and benefits of medicinal cannabis, and when and how it should be prescribed. The following resource is intended as a starting point to help navigate these shared discussions and to enable informed decision-making with patients and their whānau.

KEY PRACTICE POINTS:

- The Medicinal Cannabis Scheme came into effect on 1 April, 2020 with the aim of improving access to medicinal cannabis products by lifting regulatory barriers to prescribing. There are now two main pathways for prescribing medicinal cannabis:
 - **Medicinal cannabis products approved for distribution under the Medicines Act 1981** can be prescribed to any patient by an authorised prescriber* for any indication within that prescriber's scope of practice. Medicinal cannabis products, that are controlled drugs (e.g. Sativex), require Ministerial approval to prescribe. All registered medical practitioners (i.e. doctors) have been granted Ministerial approval to prescribe Sativex without the need to submit an application to the Ministry of Health.
 - **Medicinal cannabis products that are not approved, but that are verified by the Medicinal Cannabis Agency as meeting minimum quality standards**, can be prescribed to any patient by a medical practitioner for any indication within their scope of practice, without the need to seek approval to prescribe from the Ministry of Health. These prescriptions must be directly supplied to the patient by the prescribing medical practitioner, or dispensed via a pharmacy under Section 29 of the Medicines Act 1981.
 - Approved medicinal cannabis products and products verified as meeting the minimum quality standard are listed at [the Ministry of Health website](#)
 - Medical practitioners can still prescribe medicinal cannabis products that are neither Medsafe approved nor verified by the Medicinal Cannabis Agency. However, these have no official New Zealand endorsement of efficacy, safety or quality, and there are more restrictive access requirements, particularly if the product meets the definition of being a controlled drug.
 - No medicinal cannabis products are currently funded by PHARMAC
 - Unapproved medicinal cannabis products and controlled drugs cannot be advertised to the public in any way (including pricing information on websites). This restriction applies to any potential advertiser, e.g. suppliers, wholesalers and healthcare practitioners.
 - There is currently insufficient clinical trial evidence to support medicinal cannabis products being used first-line for any indication. However, they may be suitable for some conditions if patients have ongoing symptoms despite optimal use of conventional treatments or where other medicine use is contraindicated or not tolerated.
 - Healthcare professionals should familiarise themselves with the evidence (see links in document) regarding medicinal cannabis as this will help guide informed discussions with patients about whether treatment is suitable, balancing the safety and efficacy potential against individual patient characteristics and history
 - If a decision is made to prescribe medicinal cannabis, an initial 4–12-week trial should be undertaken based on a detailed treatment plan, including agreed upon objectives, and a plan for discontinuation if these are not achieved
 - Ensure that the prescription is written by brand as the majority of medicinal cannabis products are unapproved medicines. The brand selected should be the specific one researched during the decision-making process, as the quality, safety and efficacy may differ between products.
 - Prescriptions for medicinal cannabis products that are either approved medicines (e.g. Sativex) or verified as meeting the medicinal cannabis minimum quality standards can be dispensed at pharmacies much like other prescription medicines
- * Section 2(1) of the Medicines Act 1981 defines an authorised prescriber as a nurse practitioner, an optometrist, a medical practitioner, dentist, a registered midwife or a designated prescriber.

A brief history of medicinal cannabis in New Zealand

The unauthorised import, manufacturing and dealing of cannabis has been illegal in New Zealand since the implementation of the Dangerous Drugs Act 1927.¹ At the time, this law was enacted due to mounting international concerns over illicit drug trafficking; however, there was a provision in the law that permitted cannabis to remain available as a prescription medicine.^{1,2} The New Zealand government passed further legislative restrictions over time to broadly combat illicit drug supply and use, and cannabis was subsequently designated as a controlled drug under the Misuse of Drugs Act 1975.¹ These changes meant that medicinal cannabis could only be prescribed by a specialist with Ministerial approval.¹

Some people living in New Zealand self-medicate with cannabis regardless of the legal status

Cannabis consumption remains widespread in New Zealand, with 11–15% of adults reporting they had consumed it at least once in the last 12 months.^{3,4} Of these users, more than 40% reported that they self-medicate with cannabis to treat pain or other conditions, rather than seeking guidance from a medical professional.³ This represents a significant health issue as the quality and psychoactive content of illicitly procured cannabis can vary substantially, putting the person at an increased risk of harm. It also potentially indicates they are not accessing conventional evidence-based medicines and other treatments, further contributing to inequities in healthcare outcomes. Māori in particular have consistently experienced higher rates of cannabis-related harm and prosecution compared with other ethnic groups.¹

The shifting perspective on personal cannabis use

Public interest in pharmaceutical-grade medicinal cannabis heightened in New Zealand after several highly publicised cases of people applying for access to cannabis products for treating conditions such as severe epilepsy, multiple sclerosis and chronic pain. In late 2010, Sativex became the only available medicinal cannabis product with consent for distribution (approval) under the Medicines Act 1981, and it could only be prescribed as an add-on treatment for patients with moderate to severe spasticity associated with multiple sclerosis. Any prescribing of Sativex for off-label (unapproved) use – or prescribing any unapproved medicinal cannabis products that were controlled drugs – required case-by-case Ministerial approval under the previous regulations.

In recent years, amendments have been made to the Misuse of Drugs Act to reflect the shifting perspective that personal drug use is a health issue rather than criminal.⁵ In 2018,

changes were introduced to provide for a statutory defence for the possession of illicit cannabis by terminally ill patients, and cannabidiol (CBD) products were reclassified to no longer be controlled drugs (see: “The terminology associated with medicinal cannabis”).⁵ The following year, further amendments were made requiring Police to exercise discretion in deciding when to prosecute for the possession and use of controlled drugs.⁵ Although recreational cannabis use remains illegal, this approach shifts the focus of prosecution towards individuals who profit from drug dealing, rather than users themselves. In addition, these amendments were intended to be a first step in improving access to medicinal cannabis.⁵

The Medicinal Cannabis Agency: improving access to quality products

On 1 April, 2020, the Misuse of Drugs (Medicinal Cannabis) Regulations 2019 came into force, enabling the implementation of the Medicinal Cannabis Scheme (The Scheme).⁶ This provides a framework for a licenced domestic industry for the cultivation, manufacture and supply of medicinal cannabis, and sets the minimum quality standard which all medicinal cannabis products must meet. The Scheme is administered by the Medicinal Cannabis Agency (part of the Ministry of Health) and aims to minimise barriers and improve patient access to quality medicinal cannabis products.^{6,7} Any product verified as meeting the minimum quality standard does not require further Ministerial approval to prescribe, even if it is classified as being a controlled drug.

Evidence from other countries including Canada and The Netherlands show that government-led programmes to control medicinal cannabis production and integrate use into the healthcare system can be beneficial.⁸ The introduction of New Zealand’s Medicinal Cannabis Scheme:^{8,9}

- Permits evidence-based discussions with patients regarding the suitability and reasons for using medicinal cannabis
- Ensures product quality, consistency, and reduces the risk of product contamination
- Enables the monitoring of the patient’s response to treatment if prescribed, including both beneficial and adverse effects
- Allows New Zealand to meet its obligations under the Single Convention on Narcotic Drugs, 1961; this includes establishing an agency to control the commercial production and supply of cannabis for medical use, and reporting on the volumes of production and manufacture to the International Narcotics Control Board

Summary of the Medicinal Cannabis Scheme: how does this affect prescribing?

With the implementation of the Medicinal Cannabis Scheme, medicinal cannabis products can now be prescribed by a **registered medical practitioner** (i.e. doctor) to any patient under three main categories (Figure 1):^{6, 10}

1. **Medicinal cannabis products that are approved medicines, i.e. with Medsafe approval (or provisional approval)** can be prescribed by any authorised prescriber* for any indication within the prescriber's scope of practice. Medicinal cannabis products, that are controlled drugs (e.g. Sativex), require Ministerial approval to prescribe. All registered medical practitioners (i.e. doctors) have been granted Ministerial approval to prescribe Sativex without the need to submit an application to Ministry of Health

* Section 2(1) of the Medicines Act 1981 defines an authorised prescriber as a nurse practitioner, an optometrist, a medical practitioner, dentist, a registered midwife or a designated prescriber.

2. **Unapproved medicinal cannabis products verified as meeting the minimum quality standards by the Medicinal Cannabis Agency** can be prescribed to any patient by a medical practitioner for any indication within their scope of practice, without the need to seek approval to prescribe from the Ministry of Health. These prescriptions must be directly supplied to the patient by the prescribing medical practitioner, or dispensed via a pharmacy under Section 29 of the Medicines Act 1981.

- Products verified as meeting the minimum quality standard are listed at: www.health.govt.nz/our-work/regulation-health-and-disability-system/medicinal-cannabis-agency/medicinal-cannabis-agency-information-health-professionals/medicinal-cannabis-products-meet-minimum-quality-standard
- These medicinal cannabis products can be obtained from licenced wholesalers in New Zealand.

3. **Unapproved medicinal cannabis products NOT verified as meeting the minimum quality standards by the Medicinal Cannabis Agency** can still be prescribed by a medical practitioner and directly supplied to the patient by the prescribing medical practitioner or dispensed by pharmacy via Section 29 of Medicines Act. However, unless the product fits the definition of being a CBD product (see: "The terminology associated with medicinal cannabis") it is a controlled drug and subject to corresponding restrictions under Regulation 22 of the Misuse of Drugs Regulations 1977. Therefore, an [application](#) for a named patient must first

be approved by the Minister of Health (delegated to the Ministry of Health) for a specified indication prior to prescribing.

- These medicines also have more restrictive access criteria (for more information see: Figure 1 and "Access and dispensing considerations")

Prescribing by other types of registered prescribers

While it is anticipated that the majority of prescribing of medicinal cannabis will be undertaken by medical practitioners (i.e. doctors), medicinal cannabis products that are an approved medicine and a controlled drug, e.g. Sativex, may be prescribed in some instances by other registered prescribers, including:

- **Nurse practitioners** – an [application](#) to prescribe for a named patient must first be approved by the Minister of Health (delegated to the Ministry of Health). It can only be used for the specified indication, and prescriptions can be for no more than a one-month supply.
 - N.B. Designated nurse prescribers cannot prescribe medicines containing THC.
- **Designated pharmacist prescribers** – an [application](#) to prescribe must first be approved by the Minister of Health (delegated to the Ministry of Health). THC is listed in Schedule 1B of the Misuse of Drugs Regulations 1977. Prescriptions can only be for a specified condition and the period of supply must be no longer than three days.^{11, 12}

Only registered medical practitioners can prescribe unapproved medicines, even if verified as meeting the minimum quality standard, because unapproved medicines must be supplied under Section 29 of the Medicines Act, and these prescriptions can only be written by a doctor.¹³

Initiating the discussion around medicinal cannabis: how does it work and when might it be considered?

The endocannabinoid system as a potential treatment target

The human endocannabinoid system (ECS) is comprised of endogenously produced cannabinoids, the enzymes affecting their metabolism, as well as a widespread network of cannabinoid receptors, e.g. CB₁ and CB₂.¹⁶ CB₁ receptors are predominantly concentrated in the brain and central nervous system (CNS) but are also found in non-neural tissue, e.g. the gastrointestinal tract, lungs, kidney and liver.¹⁶ CB₂ receptors are found at a much lower level than CB₁ receptors in the CNS, and instead are mainly expressed in peripheral immune cells and tissues, and in haematopoietic cells.¹⁶ Evidence from *in vitro* and animal-based studies has shown that binding of

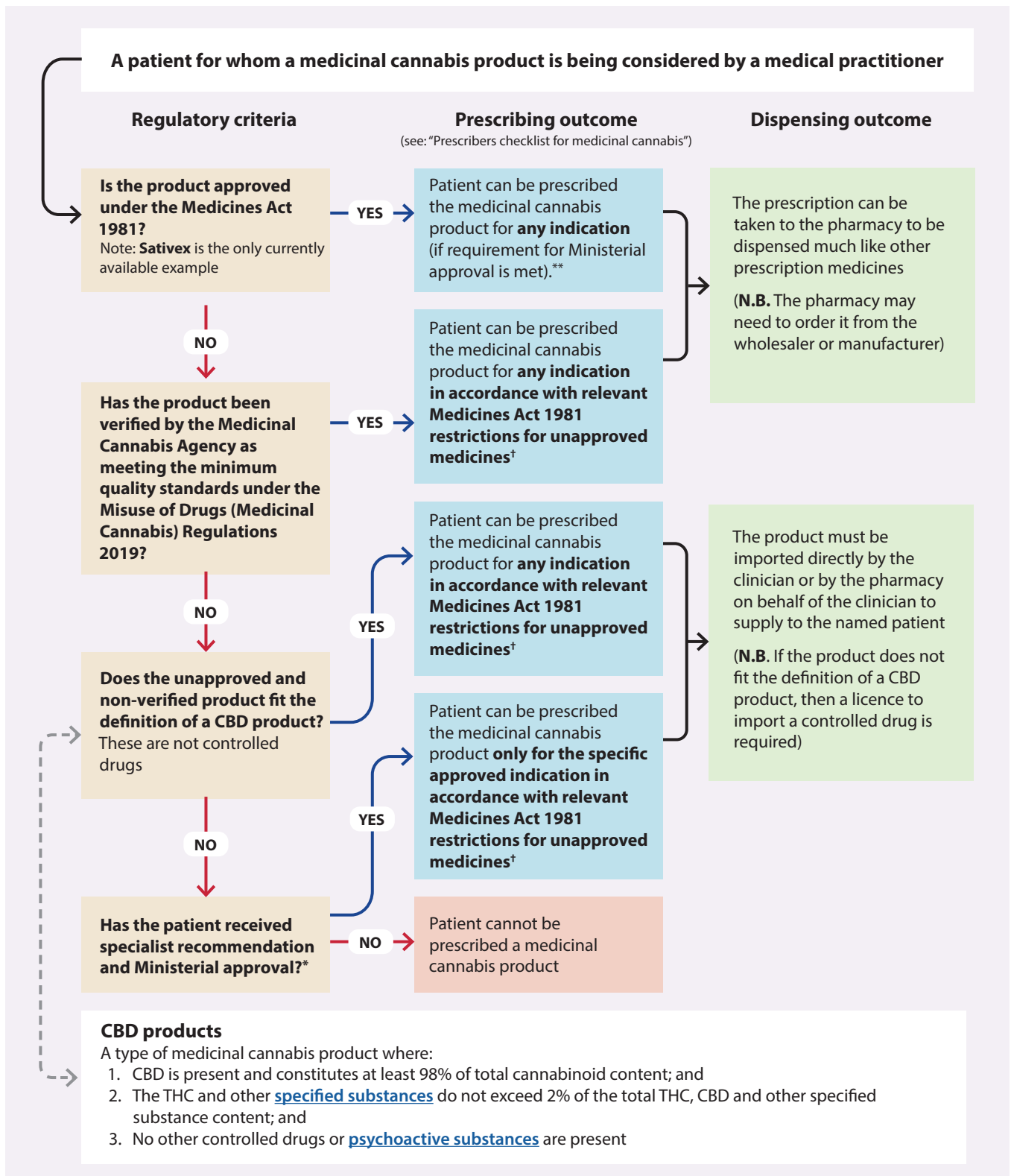


Figure 1. How the new regulatory framework affects the prescribing of medicinal cannabis products by registered medical practitioners (i.e. doctors) in New Zealand.^{6†}

* An [application form](#) for Ministerial approval to prescribe non-pharmaceutical grade medicinal cannabis without consent for distribution is available on the [Ministry of Health website](#). The application must be completed by a specialist who is managing the condition that the product is intended to treat or by the Chief Medical Officer of a District Health Board.

† Unapproved medicines must be prescribed by a medical practitioner, and directly supplied to the patient by the prescribing medical practitioner, or dispensed by a pharmacy via Section 29 of the Medicines Act.

** All registered medical practitioners (i.e. doctors) have been granted Ministerial approval to prescribe Sativex without the need to submit an application to the Ministry of Health.

‡ As of February 2022, Sativex is the only medicinal cannabis product approved under the Medicines Act 1981. All registered medical practitioners (i.e. doctors) have been granted Ministerial approval to prescribe Sativex without the need to submit an application to the Ministry of Health (see: <https://gazette.govt.nz/notice/id/2020-go997>). In addition, doctors are currently the only group that can prescribe unapproved medicines for supply under Section 29. Therefore, it is expected that doctors will be the predominant group writing prescriptions for medicinal cannabis products.

endocannabinoids, phytocannabinoids (plant-derived) or synthetic cannabinoids to their corresponding receptors causes biological effects across a range of functions, including:¹⁶

- The formation and storage of memory
- Neurological and cognitive development and function
- Sleep
- Mood
- Appetite and digestion
- Reproduction and fertility
- Inflammation and immunity
- Pain perception
- Cardiovascular system function

However, little is understood about how medicines affecting ECS-regulated processes actually influence disease outcomes. The foundation of many arguments promoting medicinal cannabis involve extrapolating these laboratory or animal-based findings, without substantiated evidence as to their translational effect on human-specific body system dysfunction.

Medicinal cannabis is not a first-line treatment for any indication

Given the recent changes in accessibility, some patients may incorrectly perceive medicinal cannabis products to be a highly effective treatment that has only just been made available. However, despite numerous anecdotal reports from people

Meeting the minimum quality standard is not the same as being Medsafe approved



While these changes reduce barriers to accessing medicinal cannabis, and will likely result in increased patient interest and demand, **the minimum quality standard is not an endorsement of a product's safety or efficacy**, i.e. it is not equivalent to being approved as a medicine by Medsafe. Instead, the standard recognises that a product is manufactured according to strict good manufacturing practices and meets minimum standards of quality, which:¹⁴

- Reduce the risk of harmful contaminants being present, e.g. pesticides and heavy metals, or any other ingredients that pose a high risk of harm
- Ensure products contain the correct ingredients, are manufactured to the stated concentration, and that the concentration is consistent throughout a batch
- Confirm that the product remains consistent throughout its stated shelf-life
- Ensure that the dosage form, packaging and labelling of products is appropriate and correct

Medsafe approval requires robust pharmacological data and human clinical trial results. Unless a medicinal cannabis product obtains Medsafe approval, prescribers are the 'gate-keepers' to access for patients and must take responsibility and liability for any outcome associated with prescribing an unapproved product. Therefore, it is important that healthcare providers familiarise themselves

with information regarding medicinal cannabis to help navigate discussions with patients, and to ensure that informed clinical decisions are made (see: "Balancing the potential benefits and risks associated with medicinal cannabis use").

Prescribers of unapproved medicines should first obtain the patient's informed consent, the details of which should preferably be documented in their notes. This involves the patient understanding:

- That the medicine is not approved in New Zealand, i.e. it has not been assessed by Medsafe against regulations and standards; it may be an approved medicine in other countries
- What, if any, other approved treatments are available
- The possible benefits in addition to any potential risks or adverse effects, including unknown risks
- That information about supply of their medicine will be forwarded to the medicine manufacturer or importer in New Zealand, who will subsequently forward a subset of that information to Medsafe; this information will be recorded on a database as a requirement of the Medicines Act

For more information on the medico-legal responsibilities and obligations associated with prescribing an unapproved medicine, see: [bpac.org.nz/bpj/2013/march/unapproved-medicines.aspx](https://www.bpac.org.nz/bpj/2013/march/unapproved-medicines.aspx)

The terminology associated with medicinal cannabis⁶

Marijuana – an alternative name for cannabis when it is used as a psychoactive substance; it usually refers to the dried, crushed flowers and leaves. Other colloquial names include pot, dope and weed. In the international medical literature, “marijuana” and “cannabis” are sometimes used interchangeably. However, when being used for treatment of patients in the New Zealand healthcare setting, the term “medicinal cannabis” is preferred as it reduces the pre-conceived association with recreational use.

Cannabinoid – a term describing a class of chemically related compounds capable of interacting with human cannabinoid receptors (see: “The endocannabinoid system as a potential treatment target”). Cannabinoids extracted from the cannabis plant are referred to as phytocannabinoids, however, they can also naturally occur in other plant species. Humans also produce their own endogenous cannabinoids (endocannabinoids).

The most notable phytocannabinoids are CBD and THC (see below), and much of the potential efficacy of medicinal cannabis products depends on the synergistic effects between these compounds.¹⁵ There is little evidence regarding the effects of other cannabinoids in humans, however, the majority are not psychoactive.

- **Cannabidiol (CBD)** – a non-intoxicating cannabinoid thought to modulate some of the psychoactive effects of THC; it does not generally produce a “high” or have an intoxicating effect in isolation.
- **Tetrahydrocannabinol (THC)** – the key psychoactive cannabinoid responsible for the “high” associated with cannabis use, which is a sought-after effect for recreational users. THC is also associated with a wide range of other effects, e.g. elevated heart rate, dizziness, impaired reaction time, reduced concentration and other neurological and behavioural effects.

Medicinal cannabis/cannabinoid products – describes a manufactured product containing one or more cannabis-derived ingredient(s) that is intended for therapeutic use.

In New Zealand, this can include a dried cannabis product intended for vaporisation (not smoking), or a product in a pharmaceutical dosage form (e.g. tablets, capsules, oils and oral mucosal sprays) containing one or more cannabis-based ingredient(s) and no other prescription or controlled drugs. Food containing cannabis is not permitted as a medicinal cannabis product. If the amount of THC or other **specified substances**^{*} is above a specific threshold, or if any other controlled drugs are present in the product (see: “CBD products”), it is classified as a controlled drug under the Misuse of Drugs Act 1975.

- **CBD products** – a subtype of medicinal cannabis product – sometimes referred to as a dosage product or cannabis-based ingredient – where:
 - (1) CBD is present and constitutes at least 98% of total cannabinoid content; and
 - (2) The THC or other **specified substances**^{*} do not exceed 2% of the total cannabinoid content
 - (3) No other controlled drugs or psychoactive substances are present



CBD products are not classified as a controlled drug.

* “Specified substances” refers to a list of compounds that naturally occur in cannabis, capable of inducing more than a minor psychoactive effect, by any means, in a person; THC is just one example. For further information on what constitutes a specified substance, see Section 2A of the Misuse of Drugs Act 1975. If you require clarification as to whether a particular ingredient qualifies as a specified substance, email the Medicinal Cannabis Agency: medicinalcannabis@health.govt.nz

N.B. For medical practitioners contemplating importing a product, it is recommended that a certificate of analysis is obtained from the manufacturer before importation to check that the product meets the requirements relating to specified substances (for further information on importation, see: “Access and dispensing considerations”).

asserting that medicinal cannabis products are effective, the available pool of peer-reviewed clinical trials in humans is limited, and the quality of evidence is not considered strong.¹⁷

Interpreting the significance of existing study outcomes is problematic due to:^{17,18}

- Potential bias
- Disproportionate enrolment of patients with a history of cannabis/cannabinoid consumption
- Differences in the dose, form and constituents of products between and within trials
- Small sample sizes and durations
- Heterogeneity in design
- A lack of effective blinding in randomised controlled trials (RCTs); nine out of ten patients or caregivers report being able to identify when cannabinoids or placebo are being used

Therefore, in the absence of large and robust RCTs comparing medicinal cannabis with established treatments, medicinal cannabis products cannot currently be considered a first-line option for any indication. However, trialling a medicinal cannabis product may be suitable in some cases if (1) patients experience ongoing symptoms despite optimal dosing of available evidence-based treatments, or (2) conventional treatments are contraindicated or not tolerated.

Shared and informed decision making is key

If conventional treatment options have been exhausted and a patient is interested in trialling a medicinal cannabis product, then it can be jointly discussed during an informed decision-making session where:



The patient can convey what they understand about medicinal cannabis and why they are considering its use; any misconceptions they may have regarding how it differs to illicit/recreational cannabis consumption or its benefits can then be addressed



The medical practitioner can set expectations by outlining any evidence of efficacy (or lack thereof) based on the indication and safety implications; this information can then be compared against other medicines the patient has previously taken, as well as any other pharmacological/non-pharmacological interventions that they may not have trialled yet



The appropriateness of medicinal cannabis use can be considered in the context of the patient's medical history and personal circumstances

Efficacy by indication: when could medicinal cannabis be considered?

This resource is not intended as a clinical guideline for medicinal cannabis use in New Zealand.

Regulators in other countries have critically evaluated existing literature and provided their own recommendations.



For further information on the evidence for medicinal cannabis use by indication, see:

- **Australian guidance** – <https://www.tga.gov.au/medicinal-cannabis-guidance-documents>
- **Canadian guidance** – <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners.html>

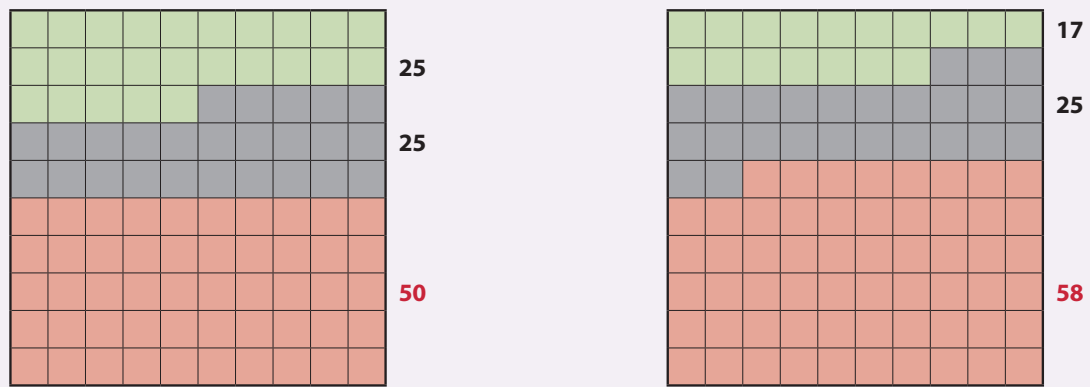


For position statements from professional healthcare organisations, see:

- New Zealand Medical Association (endorsed by the Royal New Zealand College of General Practitioners) – www.nzma.org.nz/assets/Uploads/Documents/Medicinal-cannabis-position-Statement-November-2017.pdf
- Australian and New Zealand College of Anaesthetists & Faculty of Pain Medicine – www.anzca.edu.au/news/top-news/fpm-and-medicinal-cannabis

Chronic pain. Chronic pain is the most common reason for patients enquiring about medicinal cannabis or consuming illicit cannabis.¹⁹ Meta-analyses encompassing all types of chronic pain have yielded conflicting results concerning pain improvement with medicinal cannabis.¹⁷⁻¹⁹ However, when assessed by pain subtype there is low quality evidence that medicinal cannabis may improve perceived levels of pain in patients with chronic neuropathic or malignant pain, or pain from other causes in a palliative care-setting.¹⁸ There is insufficient evidence to support routine use in patients with other types of pain, e.g. acute pain or nociceptive pain associated with rheumatic conditions (including osteoarthritis and back pain).¹⁸ There is also no evidence that adjunctive use of medicinal cannabis reduces the use of opioids in patients with chronic non-malignant pain.¹⁹

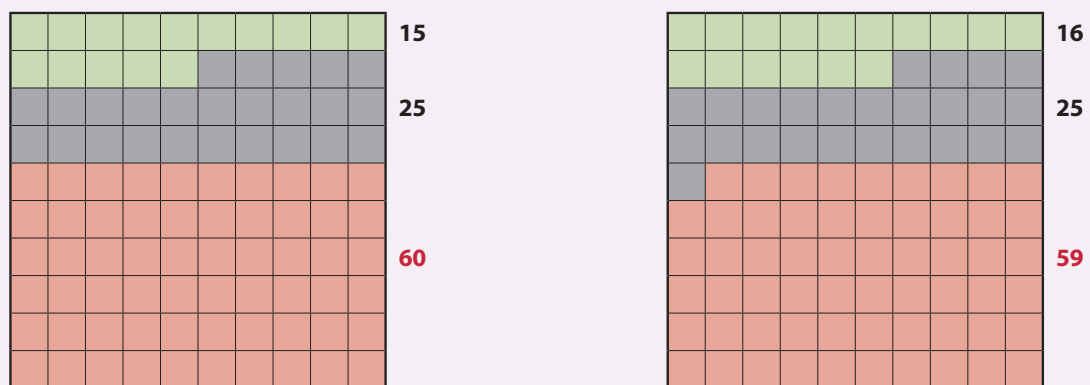
If medicinal cannabis is being considered for a patient with chronic neuropathic or malignant pain, it should be prescribed as an adjunct after discussing and trialling other options which



Amitriptyline

Venlafaxine*

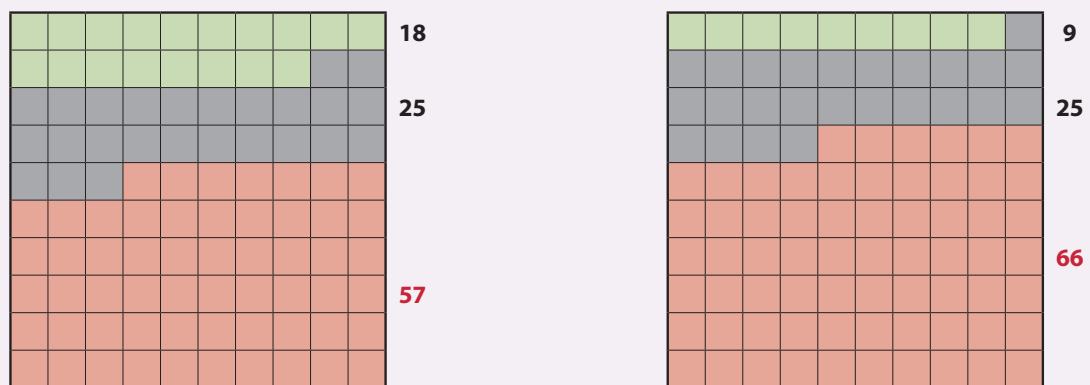
Antidepressants



Gabapentin

Pregabalin

Gabapentinoids



High-dose opioids†

Medicinal cannabis

Legend – per 100 people:
■ Improve with treatment ■ Improve with placebo or no treatment ■ No improvement

* Unapproved indication in New Zealand

† Opioids are not recommended for managing chronic non-cancer pain due to the lack of long-term efficacy, as well as the risk of harm and dependence. Doses used in this analysis were equivalent to 60 – 110 mg of oral morphine per day.

Figure 2. The efficacy of different pharmacological treatments for reducing chronic neuropathic pain by $\geq 30\%$ over 4–12 weeks. Adapted from Allen *et al*, 2018, which used indirect comparisons of data from Cochrane reviews of other neuropathic pain medications, in combination with medicinal cannabis data from their own systematic review.¹⁸

have greater evidence of efficacy and that are funded (Figure 2). Canadian guidelines suggest medicinal cannabis should only be considered after trialling:¹⁸

- At least three other medicines if the patient has neuropathic pain
- At least two medicines if the patient has malignant pain

Nausea and vomiting. There is evidence that medicinal cannabis may improve chemotherapy-induced nausea and vomiting.²⁰ However, many RCTs addressing this indication are several decades old, utilise comparator regimens no longer in use, and involve a limited duration of patient follow-up (sometimes as little as 24 hours).²⁰ There is insufficient information available to support the use of medicinal cannabis for general nausea and vomiting.¹⁷

Practice point: while it is typically associated with recreational cannabis use, consumption of products containing high levels of THC can also cause cyclic episodes of nausea and vomiting; a condition known as Cannabinoid Hyperemesis Syndrome.²¹ This condition can be difficult to distinguish from other possible causes of nausea and vomiting – and if it is not recognised – increases the risk of patients progressively self-escalating their cannabis use, which then worsens the problem.²¹ As such, medicinal cannabis use should be discontinued if nausea and vomiting persists following an initial trial (see: “Establishing a treatment plan”).

Table 1. Event rates of neurologic and cognitive adverse effects reported in randomised controlled trials for medicinal cannabis versus placebo. Adapted from Allen *et al*, 2018, which included pooled results from analyses using various THC:CBD ratios, many of which were THC-dominant or balanced formulations (i.e. not CBD products).¹⁸

Adverse effect	Medicinal cannabis	Placebo	Number needed to harm (NNH)
Sedation	50%	30%	5
“Feeling high”	35%	3%	4
Dizziness	32%	11%	5
Speech disorders	32%	7%	5
Ataxia or muscle twitching	30%	11%	6
Numbness	21%	4%	6
Psychiatric	17%	5%	9
Euphoria	15%	2%	9
Dysphoria	13%	0.3%	8
Impaired memory	11%	2%	12
Disorientation or confusion	9%	2%	15
Blurred vision or visual hallucination	6%	0%	17
Dissociation or acute psychosis	5%	0%	20
Withdrawal due to adverse effects	11%	3%	14
Overall	81%	62%	6


Spasticity. Medicinal cannabis use has consistently been associated with improvements in refractory spasticity symptoms in patients with multiple sclerosis.^{17, 22} In New Zealand, Sativex is approved as an adjunct for moderate to severe spasticity caused by multiple sclerosis.²³ The THC content in Sativex is proposed to be the important driver of efficacy for this indication through its interaction with cannabinoid receptors in the CNS.^{22, 23}

Epilepsy. There is some evidence that CBD products may help reduce the number and severity of seizures in young people with epilepsy, particularly those with Dravet syndrome and Lennox-Gastaut syndrome.²⁴ However, CBD products should only be considered as an add-on treatment in refractory epilepsy, and the decision should be guided by advice from a neurologist. Australian guidelines suggest that CBD products should only be trialled if four or five other anti-epileptic medicines have been inadequate for seizure control, either alone or in various combinations.²⁵



For children and adolescents with epilepsy, medicinal cannabis products should only be prescribed by the specialist managing their condition.

Other indications. Patients may also enquire about medicinal cannabis for other indications, however, these should only be considered on a case-by-case basis if other conventional treatment options have been exhausted. There is no compelling evidence from large clinical trials to suggest that medicinal cannabis is effective for treating the following conditions: insomnia, glaucoma, anxiety or depression, post-traumatic stress disorder, obsessive compulsive disorder, movement disorders (including tic disorder and Tourette's syndrome), anorexia, cachexia, inflammatory bowel disease, diabetes, Alzheimer's disease or schizophrenia.²⁶

 A summary of the evidence by indication (including smaller clinical trial data) can be found in "The health effects of cannabis and cannabinoids" by the National Academies of Sciences, Engineering, and Medicine, available at: <https://www.ncbi.nlm.nih.gov/books/NBK423845/>.²⁷

The potential risks of medicinal cannabis use

High quality evidence into the short- and long-term safety of medicinal cannabis is lacking. Unless medicinal cannabis products have received Medsafe approval (e.g. Sativex), they are not proven to meet international or New Zealand safety standards.

Acute toxicity is highly unlikely

There is no known level of cannabinoid ingestion that will result in a toxic or lethal dose in humans.²⁵ The median lethal dose of THC in animal models ranges from 800 to >9,000 mg/kg (depending on the species). Theoretical estimates of a lethal dose of THC for a 70 kg human range up to > 15 g.²⁸ For CBD, doses of approximately 1,000 mg/kg have been tolerated in humans.²⁵



Practice point: recommend that patients keep medicinal cannabis products in a secure location that children cannot easily access, e.g. a high or locked cupboard. Children are at an increased risk of adverse effects due to their lower body weight, and little is known regarding the safety of consumption in children aged less than five years.


Adverse effects are common but may be tolerable depending on the patient and the formulation

Overall, RCTs show that four out of five people taking a medicinal cannabis product experience some form of adverse effect.¹⁸ While direct evidence from head-to-head clinical trials is lacking, CBD products are anecdotally considered to have an improved safety profile compared with products that have a higher level of THC content, and are unlikely to induce short-term psychoactive effects, e.g. euphoria.²⁵

Common adverse effects. When initiating use or increasing the dose of any medicinal cannabis product, patients may experience transient adverse effects such as nausea, appetite changes, hypotension, gastrointestinal upset, diarrhoea and a dry mouth.²⁵ In RCTs of medicinal cannabis use, many of the reported adverse effects are mild and may be tolerable if anticipated.¹⁸

Neurological and behavioural adverse effects. The risk of more severe neurological and cognitive effects should also be a focus of any decision-making discussion with a patient (Table 1). For example, in a systematic analysis that mostly included THC-dominant or balanced medicinal cannabis formulations (i.e. not CBD products), the number needed to harm for dissociation or acute psychosis with medicinal cannabis is estimated to be 20.¹⁸ While patient reports of "feeling high" are generally associated with the use of products that have higher THC content, CBD products can still cause undesirable neurological and behavioural changes, and further investigation is required to distinguish the comparative risk.¹⁸ There is an association between the use of botanical and synthetic cannabis and long-term psychosis.²⁹ It should be emphasised that the long-term safety implications of

medicinal cannabis use is uncertain; safety data from clinical trials of medicinal CBD are relatively reassuring, however, these generally come from small cohorts studied for short durations.

 Reporting adverse effects associated with the use of medicinal cannabis products is important to further expand the understanding of their safety, particularly given the low quality of clinical trial data available to date. Any suspected adverse effects can be reported to the Centre for Adverse Reactions Monitoring (CARM) at: nzphvc.otago.ac.nz/reporting/#ReportSideEffects.

The suitability of treatment based on the patient's medical history and personal circumstances

Before making a decision to prescribe a medicinal cannabis product, the patient's history should be reviewed as this may influence the suitability of treatment.

Medicinal cannabis is generally not appropriate in people:²⁵



Who are **pregnant, planning on becoming pregnant, or breastfeeding**; pre-term labour and low birth weight have been reported, and cannabinoids can enter breast milk



With a **history of psychiatric disorders** (particularly schizophrenia), **mood** or **anxiety disorder**; Sativex is contraindicated in people with a personal or family history of psychosis or a history of another severe psychiatric disorder.³⁰ N.B. Depending on the severity of the mental illness and the reason for prescribing medicinal cannabis, there may be some occasions where the potential benefit is considered to outweigh the risk, e.g. in palliative medicine medicinal cannabis may be considered in a person with anxiety disorder, introduced in a controlled manner.



Who have **unstable cardiovascular or cardiopulmonary disease**



With a **history of hypersensitivity** to any component used in the manufacturing of the medicinal cannabis product, e.g. sesame oil, peppermint oil

Situations where caution is warranted

Hepatic or renal impairment. Cannabinoids are primarily cleared by the liver and therefore moderate to severe dysfunction will likely increase the risk of adverse effects.²⁵ Although renal function is not thought to affect clearance in healthy adults, medicinal cannabis products should be taken at the lowest effective dose in patients with chronic kidney disease.³¹ In addition, if the patient will potentially require

dialysis or a kidney transplant in the future, it is important to check with their nephrologist whether medicinal cannabis use is appropriate before prescribing.³¹

Children or adolescents. Medicinal cannabis products should typically be avoided in patients aged under 18 years due to a lack of safety and efficacy data, and uncertainty regarding the possible effects on the developing brain. There are some situations where use of medicinal cannabis may be considered in a young person, e.g. for epilepsy, but it should only be prescribed by a specialist clinician who is involved in the care of the patient for the condition being treated.

History of falls. Little is known about medicinal cannabis use in elderly or frail patients. Given that cannabinoids can decrease blood pressure and cause sedation and dizziness, this may increase the risk of falls.^{18, 25} If a medicinal cannabis product is being considered for such patients, then their home environment and level of caregiver support should be considered. If a decision is made to prescribe, treatment should be commenced at a very low dose and increased slowly.²⁵

Previous risk-associated behaviours, e.g. substance misuse disorder and drug dependence (including heavy alcohol use). Although these behaviours are not a contraindication for medicinal cannabis use per se, identifying them may (1) help shape the discussion around the intentions of seeking this type of treatment, and (2) highlight the need for safeguards to prevent excessive dosing or reliance on a product if it does not help the patient meet treatment objectives.²⁵

Psychosocial support considerations. Given that medicinal cannabis consumption can potentially cause neurological and cognitive impairment, consideration should be given to the patient's home-setting; both whether they have people to support them when initially trialling the product, and whether they have children or other dependents that may also be affected by their use, e.g. if the product causes dissociation, somnolence or acute psychosis.

Financial position. Medicinal cannabis products are not funded, and currently available options may be unaffordable for many patients. Cost may therefore result in barriers and inequitable access; for example, products may be too expensive for some patients to initially trial, or the financial burden of repeat prescriptions may be a barrier to ongoing use. This also leads to concerns that patients may seek treatment using illicit cannabis of unknown constituents and strengths.


Therefore, key concepts about cost to discuss during an informed decision-making discussion include:

- "Is there the potential for financial harm or difficulty?"

- “Would the patient be going without something necessary to afford treatment?”
- “Is there a funded medicine that has not been trialled which might be more suitable?”
- “Is the patient aware of the added risks associated with switching to illicit cannabis use if they find repeat prescriptions of legal medicinal cannabis to be too expensive?”

As competition associated with domestic cultivation, manufacturing and supply increases under the new Medicinal Cannabis Scheme, the average cost of products is expected to decrease over time. However, it is difficult to predict when this shift will occur, and whether the magnitude in price difference will make ongoing medicinal cannabis use any more realistic to those experiencing financial hardship.

Employment. The patient’s employment type should be considered during discussions, especially where driving or operation of heavy machinery is involved.²⁵ An important question to consider is: “will possible adverse effects associated with medicinal cannabis use, such as sedation, compromise their safety – or the safety of others – in the workplace?”. Employment New Zealand outlines that employers have a responsibility to create a safe work environment and “should provide employees with the highest level of protection from risks as is reasonably practicable. A risk includes dangerous behaviour resulting from drug or alcohol use”.³² However, it is unlikely that medicinal cannabis use has been considered in the development of current health and safety procedures for most workplaces.

 **Practice point:** patients should be advised not to work until it is clear how the medicinal cannabis product affects them. However, if this is not feasible, or if there is doubt about the suitability of medicinal cannabis due to a patient’s employment type, a pragmatic approach would be to offer to write a letter to the patient’s employer (with the patient’s consent) to open dialogue with them and to ensure the process is transparent.

Driving. It is illegal to drive while impaired, so depending on the type of medicinal cannabis product and the patient’s response to treatment, driving is not advised.³³ Patients initiating use of a medicinal cannabis product should refrain from driving until it is clear how the product affects them; THC is more likely to impair cognitive function, while CBD products are generally considered to have a quantity of THC that is unlikely to cause impairment.³⁴ In New Zealand, a new roadside testing scheme will be progressively phased in from late 2021 onwards, in which people will be assessed for impairment and screened for drug use via oral fluid testing.³³ THC is listed as one of the drugs being tested for under the Land Transport Act 1998 (CBD is not listed).³³ It is uncertain at this stage what

level of THC will constitute a positive test, and whether use of a THC-dominant medicinal cannabis product would meet this threshold, e.g. Sativex.^{34, 35} However, a medical defence will be available to drivers who are not impaired, but who test positive for a qualifying drug (e.g. THC) at roadside checkpoint testing if they:^{33, 35}

- Have a current legal prescription for the medicinal cannabis product
- Have complied with the instructions from the prescriber or from the manufacturer of the product about driving, consuming alcohol or other prescription medicines (or both) while consuming the product

 For further information relating to:


- Medicine use and impaired driving, see: <https://www.nzta.govt.nz/safety/what-waka-kotahi-is-doing/education-initiatives/medication/>
- Impaired driving CPD for general practitioners, see: <https://www.nzta.govt.nz/safety/what-waka-kotahi-is-doing/education-initiatives/medication/substance-impaired-driving-continuing-professional-development/>

Drug testing. In addition to roadside driver testing, patients may undergo drug testing for a variety of other reasons, e.g. workplace screening or competitive sports; depending on the setting, product and type of test or testing kit, medicinal cannabis use may result in a positive test. Products containing a higher THC content are much more likely to be detected with drug testing, particularly if a urine-based test is used.³⁶ THC can progressively accumulate in fatty tissues and slowly redistribute over time, meaning it may be detectable for days to weeks after use.³⁷ CBD products will generally not be detected using traditional testing methods.³² Cannabinoids are a prohibited substance in competition for most sports and therefore athletes should be made aware of this during initial discussions.

Consider current medicine use

Interactions between medicinal cannabis products and other medicines are possible. Both THC and CBD are inhibitors of CYP450 enzymes involved in the metabolism of numerous psychotropic medicines.³⁸ Medicines that are prominent substrates for CYP1A2, CYP2C9, CYP2C19 and CYP3A4 can have altered activity when used with cannabinoids, and close monitoring is required if they are prescribed concomitantly.³⁸ For example, the anti-epileptic clobazam is converted by CYP2C19 into an inactive metabolite, however, CBD-mediated inhibition of CYP2C19 substantially increases clobazam plasma concentrations.³⁷ It has been suggested that this interaction may account for the CBD-associated decrease in seizure frequency observed in randomised controlled trials of children with refractory epilepsy.³⁷

Other examples of medicines that may interact with cannabinoids include rifampicin, fluoxetine and warfarin.³⁸ Medicinal cannabis products may also reduce the effectiveness of systemic hormonal contraceptives, although the evidence is inconclusive.^{23, 38} Until further evidence is available, women taking a hormonal contraceptive should consider using an additional barrier contraceptive while taking a medicinal cannabis product, and continue use for three months after discontinuing the product.²³

 The New Zealand Formulary (NZF) interaction checker can be used to assess whether a patient's current medicines have potential interactions with CBD alone, CBD + THC or marijuana (*Cannabis sativa*). For further information, see: <https://nzf.org.nz/nzf/1>.

Prescribing a medicinal cannabis product

If a decision is made to trial medicinal cannabis, all current and future products that are either Medsafe approved or that are verified as meeting the minimum quality standards will be [listed on the Ministry of Health website](#). Pathways exist to prescribe products that are neither Medsafe approved nor verified as meeting the minimum quality standard, but they have more restrictive access criteria (see: Figure 1 and "Access and dispensing considerations").

The advertising of unapproved medicinal cannabis products and controlled drugs to the public is not permitted; this restriction applies to anyone, including advertising by suppliers, wholesalers and healthcare practitioners. Competition is expected to decrease prices over time, particularly once more domestic products become available. For pricing or other product details, contact the manufacturer or wholesaler directly.

CBD products can be prescribed for up to a three-month supply, while any medicinal cannabis product containing enough THC or other specified substances to be classified as a controlled drug can only be prescribed for up to a one-month supply.⁶ With the exception of the **Sativex datasheet**, there are no official New Zealand guidelines available to assist the selection of medicinal cannabis doses or formulations for specific indications. Prescribers can follow manufacturers recommendations.

Factors that may influence product selection

Route of administration. The route of administration for medicinal cannabis affects cannabinoid bioavailability and the onset of action:³⁷

- **Oral route** (e.g. oral liquid, capsule or tea) – the slowest and most variable route of absorption. Oral administration is associated with a low-level of bioavailability (~10–20%) due to intestinal and

Prescriber's checklist for medicinal cannabis products

For a patient to be dispensed a medicinal cannabis product, including CBD products, they need to have a valid prescription. The prescription must:⁶

- Be handwritten on a controlled drug prescription form (except for CBD products as they are not classified as controlled drugs), or on a personally signed barcoded controlled drug ePrescription
- Specify the brand and prohibit any generic substitutions; in some cases, prescribing software may automatically enable generic substitutions by default, so particular care should be taken to disable or remove this option if available
- Not be for a product in a form intended for smoking
- Not be for a product meeting the definition of "food" under the [Food Act 2014](#)
- Not be for a product in a sterile dosage form, e.g. eye drops
- Be prescribed for supply under Section 29 of the Medicines Act if the product is not Medsafe approved, after gaining and recording patient consent
- Be for no more than a one-month supply if a controlled drug (including Sativex)
- Be for no more than a three-month supply if a CBD product

hepatic first-pass metabolism. Effects typically occur progressively, peak two to four hours following consumption and can last for 6–24 hours; this extended duration of effect might be more desirable for patients seeking symptom control over longer periods of time, e.g. chronic pain.

- **Oral mucosal** (e.g. spray) – although it is assumed some of the product will be swallowed, this route may increase bioavailability through direct absorption through the oral mucosa. Effects likely peak after 90–120 minutes and last for a comparable amount of time to orally administered products.
- **Vaporisation** (e.g. oil or dried flower) – the most rapid onset of action, with maximum plasma concentration peaks within minutes following inhalation. Effects may reach a maximum after 15–30 minutes, and last 2–4 hours. Vaporisers can be imported and sold only if they have been approved as a medical device by an overseas regulator. Other cannabis vaporiser devices, and non-regulated utensils with [prohibited features](#), continue to be prohibited from New Zealand and may be confiscated by Customs.
- **Topical** (e.g. patches and gels) – most topical formulations produced overseas are CBD-based as CBD is approximately ten times more permeable through the skin than THC. The onset and duration of action is difficult to predict and varies substantially between patients.



Different routes of administration are associated with distinct risk profiles. When a medicinal cannabis product is verified as meeting the minimum quality standard for a specified route of administration, it only meets the standard for that particular route, i.e. a separate assessment would need to be undertaken for a product to be verified for use via other routes. If a medical practitioner wants to prescribe a medicinal cannabis product to a patient for use via an unverified route of administration, it is the prescriber's responsibility to consider the risks of using a product in a way it was not designed to be used against any potential benefits. For example, if an oral solution was verified for use via the oral route of administration but was being considered for use via the vaporisation route, considerations include:

- Whether there is any evidence the excipients in the oral liquid product are safe to be vaporised and inhaled, and whether toxic by-products may be created during heating of a product designed to be consumed as an oral formulation. Many

oral liquid medicinal cannabis products contain a carrier oil which is not intended for vaporisation, e.g. coconut oil. Products may also contain an antioxidant, e.g. vitamin E.

- The microbial contamination testing limits for products intended for vapourisation are stricter than limits applied to oral products due to increased risks with the inhaled route of administration.



For further information about the obligations of a prescriber for prescribing unapproved medicines, see: www.medsafe.govt.nz/profs/RIss/unapp.asp

The THC:CBD ratio. The label on medicinal cannabis products that have been verified against the minimum quality standard must clearly detail the THC and CBD content (including derivatives), as well as any other ingredient derived from cannabis whose content is at least 1% of the total weight or volume. THC and CBD are associated with different effects, and depending on the ratio may influence each other's biological activity.⁴⁰ Although there are anecdotal reports that certain THC:CBD ratios are more effective for specific indications (e.g. it is thought that THC content is necessary for antispastic, antidystonic and anti-tic efficacy), there is currently insufficient clinical trial evidence in humans to establish firm recommendations.⁴⁰ Australian guidelines suggest that products with low/minimal THC content are more suitable when psychoactive effects are undesirable.²⁵

Establishing a treatment plan

Once a product has been selected, establishing a treatment plan with the patient is essential to assess its effectiveness and safety, including:^{25,39}

- **Treatment objectives** – clearly document the target symptom(s) and how any improvement(s) will be assessed. For example, this may be a metric improvement in a pain score or symptom algorithm (e.g. 30%), or an objectively measured goal such as being able to perform a daily task that they were previously unable to.
- **Timeframe** – an initial one-month trial period is likely suitable to establish benefit and adverse effects. Use of the medicinal cannabis product should stop if the desired effect is not obtained after 4–12 weeks.
- **Dosing** – a good rule-of-thumb is “*start low, go slow*”. The exact starting dose and titration schedule will depend on the particular product, the balance of THC:CBD content, and patient specific characteristics. Patients taking a medicinal cannabis product for the first time without

a history of previous cannabis use should start with a very low dose and cease use if they experience adverse effects. Increasing the dose weekly is a pragmatic strategy unless the manufacturer instructions or Medicine datasheet specify otherwise (see the [Sativex datasheet](#) for further information). Dosing in the evening may be preferable for formulations with higher THC content. More specific guidance on dosing is available in the international literature,³⁹ however, caution should be taken when applying these recommendations in clinical practice.

- **Risk management strategies** – safeguards should be established. For example, if there are concerns over the potential for misuse, then dispensing frequency restrictions should be considered, and the prescriber should remain vigilant for other drug seeking behaviours, e.g. early requests for repeat prescriptions, claims of lost prescriptions, or requests for dose increases.
- **Monitoring** – clinical review should occur more frequently at first and then less frequently if the product is tolerated and stable dosing is established (based on clinical judgement). At each review, consider whether any functional and quality of life improvements outweigh reported adverse effects, and whether the patient is exhibiting undesirable behavioural or cognitive changes. There are no specific blood testing requirements. However, baseline liver function tests should usually be performed.
- **Discontinuation plan** – outline a strategy for discontinuing use if the treatment objectives are not met, e.g. a dose reduction schedule or immediate treatment cessation.

Access and dispensing considerations

As outlined in Figure 1, the Medicinal Cannabis Scheme means that if a medicinal cannabis product is a Medsafe approved medicine (i.e. Sativex) or verified as meeting the Medicinal Cannabis Agency minimum quality standard, then prescriptions can be taken to any pharmacy for dispensing. Pharmacists can then dispense the product from existing stock (if available), or obtain the product from a wholesaler or the manufacturer.⁶

Accessing medicinal cannabis products that do not have Medsafe approval or Medicinal Cannabis Agency verification against the quality standards

There are still pathways for prescribing unapproved medicinal cannabis products that have not been verified as meeting the minimum quality standard by the Medicinal Cannabis Agency under the new regulations (Figure 1). However, if such a product is selected, it should be clearly conveyed to the patient that it lacks a New Zealand-specific verification of efficacy,

safety or quality, and the responsibility for any outcome(s) lies with the prescriber. As such, these products should generally not be a first choice if there are other suitable options available.

If a **CBD product** is selected that does not meet the minimum quality standards or has not yet been assessed against the standards, then it can still be prescribed by a registered medical practitioner (i.e. doctor) for any indication within the scope of their practice, but it must be imported directly in an amount required for the named patient by the medical practitioner or a pharmacy on behalf of the registered medical practitioner.⁶ Having an expectation of future prescriptions is not considered to be a reasonable excuse to import medicinal cannabis products that have not been verified against the minimum quality standard. Given that CBD products are not controlled drugs, no additional licences are required by the medical practitioner or pharmacist. Particular care should be taken when sourcing unverified CBD products from overseas manufacturers as they may have higher THC content than is permitted under New Zealand legislation. A certificate of analysis is required from the manufacturer to confirm that the product meets the definition of being a CBD product; this should be checked by the prescriber before placing the order, and accompany the imported product to assist New Zealand border officials in their assessment.⁴¹

For other medicinal cannabis products (excluding CBD products) that do not meet the minimum quality standards or have not yet been assessed against the standards, [Ministry of Health approval](#) is required and they can only be used for the specified indication.⁶ In addition, a licence to import controlled drugs is required for each consignment, issued by Medsafe (for further information, [email Medicines Control](#)).⁶ The product must be imported directly in an amount required for the named patient by the registered medical practitioner (i.e. doctor) or a pharmacy on behalf of the registered medical practitioner.

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