

Medicinal Cannabis Products.

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What is it?

Medicinal cannabis products are made, derived, or synthesised from the cannabis plant and used under medical supervision to treat a range of health conditions.

It is critical not to confuse the non-prescribed use of cannabis with the *medicinal* use of cannabis.

Medicinal cannabis products are produced to strict quality standards, contain known ratios of cannabinoids (the active chemicals), and are taken under the supervision of a medical practitioner.

There are two primary types of medicinal cannabis products: pharmaceutical cannabis preparations, and herbal cannabis products that are grown under specific standards called Good Manufacturing Practice (GMP) to ensure consistency and quality.¹

How people use medicinal cannabis products varies, with different methods of delivery. These include smoking herbal cannabis, inhaling herbal cannabis via a vaping device, using cannabis oil (via inhalation or ingestion), buccal (oral) sprays, capsules, suppositories, pessaries and transdermal patches.

Rather than regard medicinal cannabis products as one type of medicine, they should be thought of as a ‘family of medicines’ derived from, or based on, the cannabis plant.²

Cannabinoids are present in dried cannabis flowers and may also be extracted from the plant or synthesised in a lab. The cannabis plant contains hundreds of chemicals including phytocannabinoids (cannabinoid molecules that come from the plant).

The most known and studied phytocannabinoids are:

- THC (tetrahydrocannabinol); which is responsible for the psychoactive effects of cannabis
- CBD (cannabidiol); which is not psychoactive.

Cannabis plants also contain a range of aromatic terpenes and flavonoids that may have biological effects.

Cannabinoids can be extracted or synthesised to create pharmaceutical preparations with known levels and ratios of cannabinoids. The choice of medicinal cannabinoids prescribed will depend on the believed or known efficacy of the product for the illnesses being treated.

The Therapeutic Goods Administration (TGA) provides a range of information about medicinal cannabis products for both patients and prescribers, including guidelines to help prescribers identify who may benefit from medicinal cannabis products.³

While there is understandable public interest in emerging cannabis medicines, some challenges remain in prescribing and accessing medicinal cannabis products in Australia.⁴ Most rigorous cannabis research is still in its infancy and long-term effects require further rigorous research.



Current complexities

The strong public interest in medicinal cannabis products is outstripping many doctors' education on, and our scientific knowledge of, the safety and efficacy of medicinal cannabis products in managing certain conditions.

There are a range of complicating factors associated with medicinal cannabis products research and prescribing, including:

- The discovery of the bodily system that cannabis interacts with, called the endocannabinoid system, is a relatively recent one, with most key discoveries occurring in the early 1990s. Consequently, many practicing physicians may not have received any education or training on it.
- Medicinal cannabis products are not a uniform substance, and 'the composition of cannabis preparations can be hugely variable'⁵ in terms of plant extracts, plant matter, or synthetics, as well as the amount and ratio of cannabinoids that they contain.
- Research on the safety and effectiveness of cannabinoids is of variable quality. This is in part because it has been historically difficult to conduct research and the lack of pharmaceutical industry interest in funding this research.
- Challenges have existed in running large scale trials, as intellectual property surrounding the cannabis plant is a complex space and hasn't necessarily promised a direct return on investment for pharmaceutical companies.⁵

As with any medication - from birth control pills to antidepressants - the variability of human biology means that the effectiveness of cannabinoids will also vary between individuals.⁶ Medicinal cannabis products may be effective for one person but have no benefits, or cause significant side-effects, in another.

Physicians are best placed to determine the appropriateness of treatment with medicinal cannabis products based on their patient's current needs and medical history.

Doctors need to be given accurate information about prescribing appropriate products so they can manage patient expectations about the benefits. This education and support is critical to enable physicians to develop the best possible relationship with their patient; engage in shared decision making; and, ensure that patients give free and informed consent to the use of cannabinoids.⁷

A variety of resources have been produced for patients and prescribers, including guidance documents produced for the TGA, information by Australian Prescriber including a podcast,⁸ RACGP webinars,⁹ the NSW Cannabis Medicines Prescribing Guide,¹⁰ and resources from NPS Medicinewise.¹¹

As of February 2021, Health Cert Education also offers an online Professional Diploma Program in Medicinal Cannabis, which has been reviewed by Griffin University and endorsed by the RACGP.¹²

Prescribing pathways

Medicinal cannabis products are currently available in Australia through the TGA's Special Access Scheme (SAS) and the TGA's Authorised Prescriber Scheme.

Most prescriptions are made through SAS,¹³ which facilitates prescribing through either:

- Category A: for medical practitioners on behalf of seriously ill patients
- Category B: for medical practitioners if patients do not fit SAS-A definitions. The application to access medicinal cannabis products must include a patient diagnosis, a clinical justification for the proposed use, and safety and efficacy data. SAS-B is the most common path for prescribing medicinal cannabis products.

(Note: under the 'Special Access Scheme' for unapproved medicines, the TGA does not endorse the use of, or accept responsibility for, any adverse consequences of treatment.)

The Authorised Prescriber Scheme (APS) facilitates prescribing to a predetermined class of appropriate patients with approved treatment conditions, such as paediatric epilepsy, multiple sclerosis, and palliative care.

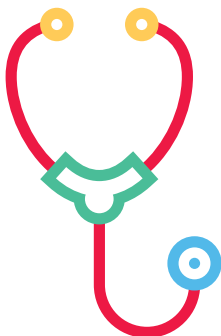
Some patients may also be able to access medicinal cannabis products through a clinical trial if their clinical condition is currently being studied and they meet the study inclusion criteria.

In Australia, clinical trials are underway for a variety of diagnoses.

In 2019, the Australian Government announced \$3 million to examine the benefits of medicinal cannabis products for managing pain and reducing symptoms and side effects of cancer patients.¹⁴

There are also a range of trials investigating treatment of insomnia, anxiety, methamphetamine dependence, post-traumatic stress disorder, and Tourette syndrome.¹⁵

These trials are essential for building the evidence base relating to the appropriate and safe clinical use of medicinal cannabis products, their efficacy, and side effect monitoring. More information about clinical trials, including current and upcoming trials, can be found on the Australian Clinical Trials webpage.¹⁶



Administering medicinal cannabis products

Medicinal cannabis products can be prepared and taken in a range of ways, with each having benefits and drawbacks.

Table 1: Delivery methods

Smoking	Rapid onset (minutes); short duration (2-4 hours); inefficient delivery as significant THC is lost during combustion and inhalation; difficult to track how much of a cannabinoid has been ingested. Smoking any product can damage the lungs. Not recommended. ³
Vaporising	Heats plant matter to a lower temperature than smoking, releasing vapour that contains fewer toxins than cannabis smoke; very rapid onset (90 seconds); short duration (2-4 hours) may be useful when immediate effects are required; no vaporisers are currently TGA approved. ³
Oils and liquid capsules	Slow onset (30-90 minutes); long duration (8-24 hours); low bioavailability; may be useful in a similar way to other long-acting medications. ³ <ul style="list-style-type: none"> • Cannabidiol - brand names: Epidyolex (Australia)/Epidiolex. • Synthetic THC, 'dronabinol' - brand names: Marinol, Syndros.
Oro-mucosal sprays	Slow onset (90 minutes); long duration (8-24 hours). ³ <ul style="list-style-type: none"> • THC:CBD, 'nabiximols' - brand name: Sativex.
Topical	Research into this route of administration is required. THC appears poorly absorbed via skin; CBD appears to be better absorbed; the onset and duration of effects is unknown. ³

Available products in Australia

More than 100 different medicinal cannabis products have been accessed in Australia, including dried cannabis flower, oils, and pharmaceutical preparations.¹⁷

Currently, there are two cannabis products listed on the Australian Register of Therapeutic Goods (ARTG):

- nabiximols (brand name: Sativex) which contains THC and CBD
- cannabidiol (brand name: Epidyolex) which is a CBD-only oil preparation.

Other products are considered unregistered and may contain either, or both, THC and CBD in various ratios. These products can still be accessed in Australia through SAS and APS, if the prescriber's application is approved.

Currently no medicinal cannabis products are listed on the Pharmaceutical Benefits Scheme (PBS), which means they cannot be accessed at a Government-subsidised price, making some medicines prohibitively expensive.

For a medicine to receive PBS listing, it must receive:

1. TGA approval after determining the medicine is effective and safe
2. Pharmaceutical Benefits Advisory Committee (PBAC) approval after considering effectiveness, safety and cost, including in comparison with other treatments
3. the Minister for Health's approval.

Maintaining the integrity of this approval system is important to ensure that all medications approved by the TGA have a robust safety profile.

Low dose CBD products

In 2020, the TGA down-scheduled some low-dose CBD products to Pharmacist Only Medicines (schedule 3).¹⁸ CBD is not psychoactive and has not been prohibited in some other countries, such as the UK, due to its low potential for harm.²

While consumers may seek to use low-dose CBD for health reasons, these products fall outside this paper's definition of medicinal cannabis products

as they can be used without ongoing medical supervision.

Medicinal CBD products, used to treat conditions such as epilepsy, are typically prescribed in much higher doses than Pharmacist Only Medicines and are not a replacement for a prescribed medicinal cannabis product.

The impact of stigma

Cannabis has had a long and colourful global history, and perceptions of its medicinal applications have changed over time.

In Australia, there is a high level of interest in medicinal cannabis products. However, entrenched stigma about cannabis, and medicinal cannabis products' association with illicit drug use, may deter people from seeking a prescription or disclosing that they have been prescribed medicinal cannabis products.

The Senate Community Affairs References Committee Inquiry into *'Current barriers to patient access to medicinal cannabis in Australia'*¹⁹ report suggests that stigma could be an issue when patients raised the possibility of using medicinal cannabis products with their GP or specialist.

The report notes that "at worst, the committee was told that patients were simply rebuffed and felt ostracised by the negative or dismissive attitude of the clinician they consulted."¹⁹ It states that stigma in the health profession towards medicinal cannabis products needs to change because it can undermine trust with patients.

No one should feel stigmatised for considering potential treatment with medicinal cannabis products.¹⁹

To address the stigma and increase knowledge of how medicinal cannabis products can be accessed, the Senate Community Affairs References Committee recommended:¹⁹

- developing targeted education and public awareness campaigns
- providing both online and in-person training options around medicinal cannabis products for medical practitioners
- mandatory inclusion of education on medicinal cannabis products and the endocannabinoid system in medical schools' curriculum
- developing patient-focused resources that explain how to access medicinal cannabis products.

The impact of stigma and discrimination toward people cannot be understated.

While it is illegal to promote the use of any Schedule 4 or 8 medication, appropriate information given to patients to share with others may help reduce stigma. Educating the public that medicinal cannabis products are distinct from illicit cannabis may also help to address inaccurate perceptions.

The Committee's report also states that without resources to support patients and prescribers in accessing medicinal cannabis products, "patients will continue to miss out on potentially beneficial treatment options, and, worryingly, may continue to turn to the black market in a bid to access medicinal cannabis products."¹⁹

An online survey conducted by the Lambert Initiativeⁱ two years after the legalisation of medicinal cannabis products found that 47.8% of respondents acquired cannabis products for

i Limitations of the survey design (online, convenience sampling, recruiting from online medicinal cannabis forums) might have resulted in over-estimates.

medicinal purposes from a non-prescribed source because they did not know a medical practitioner who was willing to prescribe.

Another 18.4% reported that their practitioner was not interested or was unwilling to prescribe it,

and 12.7% preferred to keep their use of cannabis confidential from their doctor.¹⁷ Other reasons included not knowing cannabis could be legally prescribed (32%), its prohibitive cost (21.2%) and having a preference for illicit cannabis (9.5%).¹⁷

Australian guidance for medicinal cannabis products

In Australia, cannabis is not recommended as a first-line therapy for any ailment.

Rather, it is suggested as a treatment to try when other approved medicines have been unsuccessful.³

There are no limits on the conditions for which medicinal cannabis products can be prescribed in Australia.

This means that, despite the current guidance, Australian patients may seek - and potentially be granted - access to medicinal cannabis products for the conditions included in this paper as well as others that are not listed. This can be done on a case-by-case basis through the Special Access Scheme.

General dosing guidance is to “start low, go slow”.³

As with all medicines, adverse reactions do occur to medicinal cannabis products and there are potential interactions between cannabinoids and other drugs that are still being investigated.

Medicinal cannabis products which contain THC are not recommended for patients with a history of mood, anxiety, or psychotic disorders;ⁱⁱ for people who are pregnant or breastfeeding, or for those with “unstable cardiovascular disease”.³

The TGA has published a series of guidance documents around medicinal cannabis products for specific conditions. It is important to note that these are for guidance only and do not constitute clinical guidelines due to the lack of evidence for many of the proposed medical uses.

Guidance is provided on:

- paediatric and young adult epilepsy
- multiple sclerosis
- chronic non-cancer pain
- palliative care
- nausea and vomiting.

Please see appendix for details on this guidance.

Medicinal cannabis products internationally

More than 50 countries have approved medicinal cannabis products access schemes.

The nature and regulations of these schemes vary considerably – some countries only allow access to pharmaceuticals such as Sativex or Epidiolex, others only permit access to CBD and/or low THC products, while others allow for

a wide range of preparations as well as access to herbal cannabis.²⁰

Some countries restrict prescribing medicinal cannabis products to a limited range of conditions, such as cancer, while others have extensive lists of conditions for which it can be prescribed.²⁰

ii This guidance does not exclude people with those conditions from participating in clinical trials that are recruiting for the study of cannabis and those conditions.

ADF positions

1. In areas where the evidence is limited or weak, there is a need for investment in research that can support evidence-based clinical decision making.
2. Because rigorous cannabis research is still in its infancy for many proposed medical uses, the ADF supports the current Australian regulatory regime for medicinal cannabis products, noting that it has only been in place since 2016.
3. Any changes to the role and use of medicinal cannabis products for the management of indicated conditions should be supported by appropriate evidence-based education, professional and organisational development, and the development of evidence-based clinical guidelines. This is to support general practitioners and clinicians to use medicinal cannabis products in a safe and effective way that is aligned to best practice standards, improves patient access, and reduces the stigma associated with seeking and accessing medicinal cannabis products.

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Appendix A: TGA guidance on specific conditions

This guidance was informed by reviews of the research conducted by an academic team co-ordinated by the National Drug and Alcohol Research Centre. The guidance documents were developed by clinicians within the TGA in consultation with a broad range of Australian organisations including:

- 18 patient and consumer representative groups
- all state and territory health departments
- 15 health care professional organisations
- clinical staff from 29 hospitals and health care systems
- 14 outpatient or primary health networks.²¹

It is important to note that these are to provide guidance only. They are not clinical guidelines because of the absence of evidence for many of the proposed medical uses for medicinal cannabis products. Links to the evidence reviews are provided at the bottom of each condition.

Paediatric and young adult epilepsy

Epilepsy is a neurological disorder in which patients experience seizures. While some people may only experience a single seizure, others will experience unprovoked, recurring seizures. There are many types of epilepsy which range in symptoms and severity. Treatment focuses on:

- reducing seizure frequency
- improving quality of life
- ideally achieving freedom from seizures.²²

The use of CBD to manage paediatric epilepsy has been of particular interest in research. While current evidence is complex and evolving, it is promising for some patients with drug-resistant epilepsy.

The guidance document reports that of the two double-blind RCTs, one found 42.6% of participants and the other found 44.2% of participants achieved a 50% or greater reduction in seizures by adding CBD (cannabidiol) to their existing treatment.²²

The synthesis of the quantitative evidence conducted for the guidance included 35 papers on 36 individual studies.²²

Australian guidance:

“Epilepsy treatment with medicinal cannabis or cannabinoids is only recommended as an adjunctive treatment – that is, in addition to existing anti-epileptic drugs.”²²

A pharmaceutical preparation of CBD, called Epidyolex, is now listed on the Australian Register of Therapeutic Goods (ARTG) and is being considered for listing on the PBS.

Full review: <https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-treatment-epilepsy-paediatric-and-young-adult-patients-australia>

Multiple sclerosis

Multiple sclerosis (MS) is a disease that affects the central nervous system. There is currently no cure for MS and the speed and nature in which the disease progresses differs between patients.

Common symptoms of MS that researchers hope cannabis might be useful in treating include:

- disability and disability progression
- pain
- spasticity
- bladder function
- ataxia and tremor
- sleep
- quality of life.²³

The systematic review-of-reviews conducted for the guidance included 11 systematic reviews on 32 individual studies.²³

Australian guidance:

“There is some evidence that dronabinol or THC extracts may be effective at reducing pain associated with multiple sclerosis. There is also some evidence (although inconsistent) that nabiximols and other THC:CBD extracts may reduce muscle spasticity and improve patient quality of life.

“Recommendations are limited by lack of quality evidence. Currently available studies demonstrate no evidence of an effect of cannabinoids on MS disease activity or disability progression. There have been no studies comparing cannabinoids against current standard treatments for multiple sclerosis.”²³

A pharmaceutical preparation of a 1:1 ratio of THC to CBD, nabiximols (Sativex), is listed on the ARTG as a treatment for muscle spasticity associated with MS. However, it has twice been rejected from listing on the PBS because the treatment effect is considered to be likely overestimated and there is a lack of evidence for cost-effectiveness.²⁴

Full review: <https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-treatment-multiple-sclerosis-australia>

Chronic non-cancer pain

People may experience chronic non-cancer pain (CNCP) for a range of reasons, including unknown causes. Untreated chronic pain can severely impact a person’s quality of life and capacity for employment, leisure, and social activities.

Specific chronic pain conditions discussed in the guidance document include:

- neuropathic pain
- fibromyalgia
- arthritis.²⁵

Thirty-four publications were included in the CNCP quantitative synthesis conducted for the guidance document. Ninety publications in total, covering 102 studies were analysed, including 34 on CNCP, 50 on neuropathic pain, two on arthritis, and four on fibromyalgia.²⁵

Australian guidance:

“A comprehensive sociopsychobiomedical assessment of the patient with CNCP is appropriate.

“The use of medications, including medicinal cannabis, is not the core component of therapy for CNCP.

“Patient education is a critical component of therapy for CNCP, particularly with respect to expectations of drug therapy.

“There is a need for larger trials of sufficient quality, size and duration to examine the safety and efficacy of medicinal cannabis use in CNCP.”²⁵

There is conflicting research evidence on whether medicinal cannabis products used as a supplement to opioids in the treatment of CNCP reduces the need for opioids to achieve pain relief. Studies into this potential effect are underway but there is currently insufficient high-quality evidence.²⁵⁻²⁹

Full review: <https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-treatment-chronic-non-cancer-pain-australia>

Palliative care

Palliative care is person and family-focused support for those with a terminal illness. Palliative care addresses physical discomfort and the emotional, social, and spiritual needs of the individual and their family.

There is very limited evidence on the use of medicinal cannabis products in palliative care. The care required is highly individual, so services provided vary greatly between people and the nature of their terminal illness. When a palliative care patient expresses interest in cannabis, it is suggested that their physicians encourage the patient to enrol in a clinical trial if possible.³⁰

Australian guidance:

“As there are very few studies on medicinal cannabis products treatment in palliative care, it should be used only after standard treatments have failed. It is possible that medicinal cannabis products will interact with chemotherapy and other medications used in palliative care. More studies are needed to better understand this.”³⁰

Full review: <https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-treatment-palliative-care-patients-australia>

Nausea and vomiting

Nausea and vomiting may occur for a range of reasons, including:

- induced by chemotherapy or radiation therapy
- associated with cancer or various chronic diseases
- post-operational
- side effect of some medications.³¹

Eleven studies were included in the systematic analysis conducted for the guidance document. The guidance notes that there are newer, much more effective antiemetic medicines now prescribed than the drugs that medicinal cannabis products were originally compared to.³¹

Australian guidance:

“High-THC medicinal cannabis products can sometimes be effective for nausea and vomiting and should only be prescribed after newer standard approved treatments have failed and where otherwise not contraindicated.”³¹

Full review: <https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-prevention-or-management-nausea-and-vomiting-australia>

Appendix B: How medicinal cannabis products work

Medicinal cannabis products work by interacting with our body's endocannabinoid system.

The human body features a number of inter-related systems, like the digestive system and the immune system, that work together to keep us alive. For example, the respiratory system uses our lungs to capture oxygen that is then passed into our blood, and the cardiovascular system pumps our blood through the heart and around the body to distribute that oxygen.

One of these systems is the endocannabinoid system. The endocannabinoid system is very complex, and research is still uncovering exactly how it works and what it does.

The endocannabinoid system³²

The endocannabinoid system is found in all mammals, including humans, and most animals.

It has three main parts:

- chemicals naturally made by the body called endocannabinoids
- receptors that the endocannabinoids lock in to which receive and transmit signals
- enzymes that are responsible for breaking down the endocannabinoids when they've done their job.

The *Cannabis sativa* plant also produces many different cannabinoids, called phytocannabinoids, that when injected interact with the endocannabinoid system by attaching to the same receptors as the endocannabinoids made by the body.

There are two known receptors in the system. CB1 receptors are found densely within the central nervous system (brain and brain stem) while CB2 receptors are found primarily, but not exclusively, in the peripheral nervous system and immune system.

When cannabinoids – both phytocannabinoids, and endocannabinoids – interact with receptors it produces a range of effects in the body.

The range of functions of the endocannabinoid system is still being investigated but it appears to be implicated in a diverse range of processes including, but not limited to:^{32, 33}

- sleep
- mood
- memory
- appetite
- digestion
- motor control
- inflammation and related immune responses
- cardiovascular function
- liver function
- metabolism
- neurodegenerative diseases.

The fact that the endocannabinoid system affects such a wide variety of bodily processes is one reason for the wide interest in exploring the potential roles of medicinal cannabis products in the treatment of numerous illnesses.

Cannabinoids

There are many types of cannabinoids that interact with the endocannabinoid system. Different types of cannabinoids can have different effects. This is why certain illnesses might benefit from some cannabinoids, but not others.

Endocannabinoids

These cannabinoids are naturally produced by the human body. We currently know of two endocannabinoids: anandamide and 2-arachidonoyl glycerol (2-AG).³²

Phytocannabinoids

These cannabinoids are produced by the *Cannabis sativa plant*, the best-known examples of which are THC and CBD.³² However, there are more than 100 phytocannabinoids, the majority of which are still being investigated.

Synthetic cannabinoids

These ‘man made’ cannabinoids were created to mimic the effects of endocannabinoids or phytocannabinoids. They include dronabinol which is a synthetic THC and nabinol.ⁱⁱⁱ

Potential harms

Adverse reactions

THC is more likely to produce an adverse reaction than CBD.³⁴

Adverse reactions can include:

- anxiety
- panic attack
- extreme confusion and disconnection from time and the environment
- racing heart rate
- paranoia
- dry mouth
- temporary loss of motor skills and/or short-term memory
- cannabis-induced psychosis.

Dependence

Cannabis poses a risk for dependence.

Among adults who have used cannabis in their lifetime for non-medical purposes, an estimated 20% may be at risk of developing dependence.³⁵ This risk increases the more frequently cannabis is used.

The differences between medical and non-medical cannabis users and their patterns of use however, means we cannot extrapolate dependence risks from research conducted predominantly on people using cannabis for non-medical reasons.²

For example, CBD is hypothesised to possess some ‘anti-addictive’ properties.^{2,36} In contrast, high THC cannabis is understood to pose an elevated risk for dependence.² It is possible that some formulations of medicinal cannabis products, depending on the cannabinoids used, may pose a different level of risk for dependence than non-prescribed cannabis.

Furthermore, the characteristics and motivations for cannabis use by people using prescribed or non-prescribed cannabis are likely to vary and this can affect the risks of experiencing dependence.²

Withdrawal

People who regularly use cannabis may experience withdrawal symptoms when they stop using it.

These can include:³⁷

- urge to use cannabis
- sleep problems, including nightmares
- loss of appetite
- nausea
- irritability or anger.

Symptoms typically peak within one week and subside after one to two weeks.

iii These are distinct from so-called ‘legal highs’ such as K2, Spice, etc. which are largely unknown and untested formulations that may not contain cannabinoids, but often contain a plethora of pharmaceutical products which are sprayed onto plant matter.

Toxicity

There have been no known deaths due to cannabis toxicity.³⁸

Australian deaths in which cannabis is listed as a contributory cause of death include:³⁸

- accidental injury
- suicide
- polysubstance toxicity
- assault.

Driving

THC intoxication is known to decrease a person's ability to drive. In all Australian states, there is roadside drug testing for cannabis with a zero-tolerance threshold for its presence.^{39, 40} CBD is not tested for.

Patients being treated with CBD-only products may still be able to drive, as long as they are not impaired, but they should discuss this with their treating practitioner and may wish to consult the relevant road safety authority in their state or territory.^{41, 42}