



Australian Government

Department of Health

Therapeutic Goods Administration



Guidance for the use of medicinal cannabis in Australia

Patient information

Version 1, December 2017



Copyright

© Commonwealth of Australia 2017

This work is copyright. You may reproduce the whole or part of this work in unaltered form for your own personal use or, if you are part of an organisation, for internal use within your organisation, but only if you or your organisation do not use the reproduction for any commercial purpose and retain this copyright notice and all disclaimer notices as part of that reproduction. Apart from rights to use as permitted by the *Copyright Act 1968* or allowed by this copyright notice, all other rights are reserved and you are not allowed to reproduce the whole or any part of this work in any way (electronic or otherwise) without first being given specific written permission from the Commonwealth to do so. Requests and inquiries concerning reproduction and rights are to be sent to the TGA Copyright Officer, Therapeutic Goods Administration, PO Box 100, Woden ACT 2606 or emailed to <tga.copyright@tga.gov.au>.

Medicinal cannabis: patient information

In the past few years a number of Australians have expressed interest in the use of cannabis for medicinal purposes. The Commonwealth and state and territory governments have either used their current laws or passed specific laws to allow the prescribing and dispensing of medicinal cannabis products. The Commonwealth and, in some cases, state and territory governments have also passed laws allowing cannabis cultivation and manufacture for medicinal purposes.

Currently there is only limited evidence about the effectiveness of medicinal cannabis for use in different medical conditions. There is also little known about the most suitable doses of individual cannabis products.

This is why, with the exception of one product (nabiximols), medicinal cannabis products are not at this time available as a registered prescription medicines in Australia or most other countries. Most medicinal cannabis products are not registered on the Australian Register of Therapeutic Goods (ARTG).

For a particular product to become registered on the ARTG a sponsor (usually a company) would need to submit a dossier of evidence on the clinical efficacy, safety and manufacturing quality of a particular medicinal cannabis product to the Therapeutic Goods Administration. At this time, the Australian Government does not subsidise the cost of medicinal cannabis products through the Pharmaceutical Benefits Scheme (PBS).

The Australian Government Department of Health and the NSW, Victorian and Queensland state governments commissioned a team from the Universities of New South Wales, Sydney and Queensland under the co-ordination of the National Drug and Alcohol Research Centre (NDARC) to review the available clinical evidence for using medicinal cannabis. The team focused on the five areas for which the largest numbers of studies have been carried out—palliative care, chemotherapy-induced nausea and vomiting, chronic pain, multiple sclerosis and epilepsy in paediatric and adult patients.

This brochure provides a broad overview of the current evidence to support using medicinal cannabis for the above conditions. It also highlights the cautions surrounding treatment, how medicinal cannabis can be prescribed and future research. The Department of Health will update this brochure as new evidence emerges.

Currently there is only limited evidence about the effectiveness of medicinal cannabis for use in different medical conditions. There is also little known about the most suitable doses of individual cannabis products



The evidence

Doctors rely on evidence to make informed decisions about the best medications for their patients. For medicinal cannabis, the amount of evidence is currently limited and the products, doses and research methods used vary between studies. This makes it difficult to come to firm conclusions about how best to use particular medicinal cannabis products.

There is also not much information available to help doctors determine the most appropriate and safe doses while minimising potential side-effects. Importantly, at the moment, relatively few studies compare the effects of medicinal cannabis products against currently approved treatments for various conditions and symptoms. In addition, most of the studies reported in the medical literature have either used purified pharmaceutical substances or smoked cannabis.

As there is limited scientific evidence to support the use of medicinal cannabis in most conditions, and in many cases the evidence is for its use together with other medicines, it should be used only when approved treatments have been tried and have failed to manage conditions and symptoms.

Access to medicinal cannabis

Medicinal cannabis can only be prescribed by a registered medical practitioner.

Before prescribing medicinal cannabis, the doctor will assess each patient to decide if the treatment is appropriate for their condition and individual circumstances. The doctor will take a medical history and a family health history. The doctor will also consider the patient's current medications and any problems with drug dependence and substance abuse.

With the exception of one product (nabiximols), medicinal cannabis products are not registered medicines in Australia, so they must be accessed through special pathways available for unapproved medicines.

Individual consumers cannot apply to TGA to obtain approval to access unapproved medicinal cannabis products. Such access can only be arranged through an Australian-registered medical practitioner with appropriate qualifications and/or expertise for the medical condition requiring treatment. This doctor can notify/apply on the patient's behalf for



approval to import and supply these products through the Special Access Scheme (SAS Category A or B). Alternatively, the doctor can apply to us to become an Authorised Prescriber (AP). Approval or authorisation is granted on a case-by-case basis.

This doctor must also apply and obtain approval under the applicable state or territory laws to prescribe a medicinal cannabis product to a particular patient, where relevant. Rules relating to medicinal cannabis products vary between states and territories and could affect whether or not you can be prescribed particular medicines in your state or territory.

If both state and TGA requirements are satisfied then the pharmacy or hospital that the doctor has arranged to supply the product can dispense it. The medicinal cannabis products may already be available in Australia if the Office of Drug Control has authorised their import. The Office of Drug Control website (www.odc.gov.au) gives a list of companies who have been authorised to import medicinal cannabis stock into Australia for supply through SAS approvals or AP authorisation. Please note that inclusion on this list does not guarantee stock availability or automatic approval for patient access by the TGA or the states and territories.

Should the product requested not be authorised to be held in Australia then the doctor (or pharmacist/hospital on the doctor's behalf) wishing to import the product may then need to obtain import permits from the Office of Drug Control.

The products

A variety of products are current available through import from Canada or Europe. These include raw (botanical) cannabis, which for medicinal purposes should be vaporised but not smoked, cannabis extracts in oils, and solvent extracts such as tinctures, and oro-mucosal sprays. Some products for trans-dermal application (patches or topical application of gel or cream) have also been developed.

Similar products, manufactured from locally grown medicinal cannabis are expected to become available during 2018.

A challenge is that many of the studies described in the medical literature have used either smoked cannabis (which is not recommended on health grounds) or purified tetrahydrocannabinol (THC) or cannabidiol (CBD), rather than many of the types of products that are currently available internationally.



There are up to 100 cannabinoids in the cannabis plant. The cannabinoids are most abundant in the female flower head, which is used in the manufacture of medicinal cannabis products.

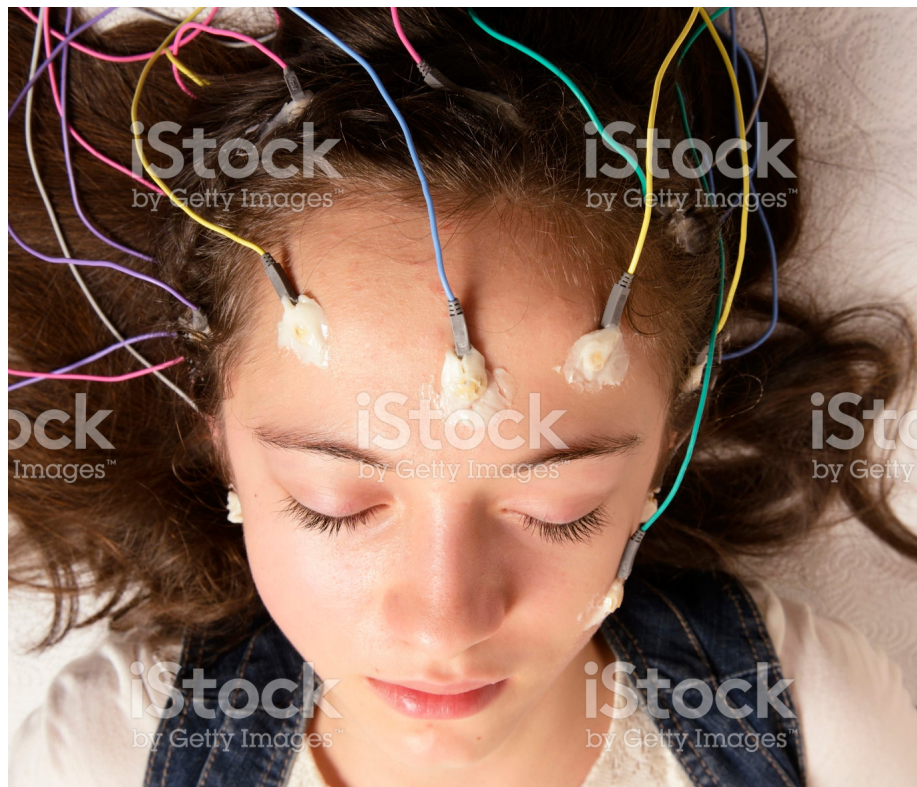
Tetrahydrocannabinol (THC) is responsible for the psychoactive effects of cannabis and is the reason cannabis is used recreationally. THC may also be responsible for some of the medicinal effects of cannabis such as reduction of nausea, vomiting, pain and muscle spasms as well as improvements in sleep and appetite.

A second cannabinoid, cannabidiol (CBD) is not psychoactive and may be useful in the management of seizures, pain, and may have anxiolytic and antipsychotic effects. Different cannabis strains contain different ratios of THC to CBD. It is unclear whether THC and CBD act individually or synergistically (in conjunction with each other). Other cannabinoids under active research include cannabigerol (CBG), tetrahydrocannabivarin (THCV), cannabinol (CBN) and cannabichromene (CBC). The cannabis plant also contains terpenes which give cannabis its flavour and aroma. It is unclear whether terpenes have their own pharmacological effects.

Medicinal cannabis and epilepsy in paediatric and adult patients

The main purpose of epilepsy medications is to reduce the number of seizures and ideally to stop them altogether. There is some evidence to support using medicinal cannabis in the treatment of certain childhood epilepsies.

There is some evidence to support using medicinal cannabis in the treatment of certain childhood epilepsies



Cannabidiol (CBD) is the substance featured in most published evidence on medicinal cannabis as an epilepsy treatment. However, this evidence is when it is used as an add-on to current treatments in drug-resistant epilepsy in children and young adults up to 25 years where use of several anti-epileptic drugs has not controlled their condition. In patients with paediatric-onset drug-resistant epilepsy, CBD products reduced seizure frequency by 50 per cent or more in up to half of the patients and achieved seizure freedom in a small number of patients. Several studies have reported improved quality of life in paediatric and adult groups, but overall there are few studies of how effective CBD is in treating adult epilepsy. There is not enough evidence to recommend this treatment for adults.

There is no evidence to support medicinal cannabis as a rescue therapy for status epilepticus (a single seizure lasting more than five minutes or two or more seizures within a five-minute period without the person returning to normal between episodes).

Information is limited on the most effective starting doses to treat epilepsy in children and young adults. As extra care is needed, it is expected that paediatric neurologists would be involved in the management of these children.

Medicinal cannabis and multiple sclerosis (MS)

There is a TGA registered medicine (Nabiximols, which are an extract of cannabis plant containing roughly equal amounts of THC and CBD) for the use in MS for muscle spasticity. Five of ten studies carried out on other cannabinoids concluded that there was evidence that cannabinoids may be effective for symptoms of pain and/or spasticity and positive effects on sleep and bladder symptoms. It should be noted that the other five studies were inconclusive or did not show that treatment with cannabinoids had any positive effect in MS.

There is some low to moderate evidence to suggest that medicinal cannabis products may be effective for treating the pain symptoms of MS, although this is inconsistent. Studies differ as to whether medicinal cannabis products can help improve bladder function, sleep, quality of life, ataxia/tremor and disability/disease progression.

There are also currently no studies that compare medicinal cannabis products to the most effective and commonly-used medications for MS pain and spasticity. Therefore, there is no evidence to support the use of most cannabinoids as a single, primary or initial treatment.

Treating doctors should assess people with MS after 12 weeks to re-evaluate and monitor both the positive and negative effects of the drug.

There is some low to moderate evidence to suggest that medicinal cannabis products may be effective for treating the pain symptoms of MS



Treating chronic non-cancer pain

There is some evidence that cannabinoids can reduce pain in both MS-related neuropathic pain and non-MS-related neuropathic pain, but for many people the reduction in pain may be modest. There is, however, insufficient information to make a conclusion about cannabinoids for the treatment of pain associated with arthritis and fibromyalgia

The majority of the studies on the use of cannabinoids in pain have studied THC or THC-rich extracts. The studies are mainly where cannabinoids were “adjuvant” treatments, used in addition to other pain medicines.

Most studies have been on chronic (long-term) rather than acute (short-term) pain. Patients and healthcare professionals recognise that there are two main types of chronic pain. Nociceptive pain, which can be found with or without cancer, is caused by damage to body tissue and usually described as a sharp, aching, or throbbing pain to the bones, muscles, or joints, or that causes the blockage of an organ or blood vessels. Neuropathic pain occurs when there is nerve damage, in particular to those nerves in the spinal cord. The pain is often described as a burning or heavy sensation, or numbness along the path of the affected nerve.

There is some evidence that cannabinoids can reduce pain in both MS related neuropathic pain and non-MS related neuropathic pain, but for many people the reduction in pain may be modest. There is, however, insufficient information to make a conclusion about cannabinoids for the treatment of pain associated with arthritis and fibromyalgia.

Current studies show no evidence that medicinal cannabis can improve overall quality of life or physical functioning. There is also some evidence that it can improve sleep.

There is much interest at present as to whether cannabinoids are “opioid sparing” – in other words, whether use of medicinal cannabis products for pain can result in a reduction of use of strong opioids. If this were the case, deaths and incapacity from opioid overdoses could be reduced, given that cannabinoids have fewer adverse outcomes. While some individuals with pain have reported that their use of opioids has been reduced when they also use medicinal cannabis, clinical studies in this area are still ongoing.



Preventing and managing chemotherapy-induced nausea and vomiting in cancer (CINV)

There are some reports that medicinal cannabis products (in particular THC and related substances) relieved the symptoms of CINV. However, the number of studies is small and the quality of published evidence is low to moderate. While several studies found that the medicinal cannabis products were as effective as the prescription medicine it was compared with, most of the research studies were carried out some years ago, and in recent years much more effective prescription medicines for nausea and vomiting have become available.

For these reasons, THC-rich medicinal cannabis products for chemotherapy induced nausea and vomiting should be prescribed only after standard approved treatments have failed.

There is no evidence at this time that medicinal cannabis has any anti-cancer activity or that it can slow the progression of these conditions

Medicinal cannabis use in palliative care

While medicinal cannabis products can be used to treat nausea and vomiting due to chemotherapy, there is little evidence of any benefit to advanced cancer patients with chronic pain. The published studies in the medical literature showed little effect on appetite, nausea/vomiting, pain, dizziness, mental health or sleep problems. There is also no evidence that medicinal cannabis has any anti-cancer activity in human studies or that it can slow the progression of these conditions.

In people without acquired immunodeficiency syndrome (AIDS), there is also no evidence that medicinal cannabis will increase their appetite, that it will help the patient gain weight or that it will enhance their mood.

It is important to note that some side-effects from medicinal cannabis treatment may be similar to symptoms of distress often experienced by people in end-of-life care.

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

People with life-limiting conditions may want to enrol in clinical trials to help increase the amount and quality of evidence to support or contradict medicinal cannabis use in this setting.



Summary of evidence by condition

Condition	Products	Current evidence quality
Multiple sclerosis		
Pain	Dronabinol , THC extracts	Low to high and inconsistent
Disability and its progression		None
Spasticity	Nabiximols and THC:CBD	Low and inconsistent
Bladder function		None
Ataxia and tremor		None
Sleep		None
Quality of life	Nabiximols and THC:CBD	Low and inconsistent
Epilepsy		
To reduce and/or eliminate the number of seizures	CBD when used in conjunction with anti-epileptic drugs	Low to very low
	Oral cannabis extracts (OCEs)	Very low
	CBD:THC	Very low
	Cannabis sativa	Very low
Quality of life	CBD	Low
	Oral cannabis extracts (OCEs)	Very low
	CBD:THC	Very low
	Cannabis sativa	Very low
	THC	Very low
Palliative care		
Alzheimer's disease	Dronabinol	Unclear
Advanced cancer symptom control	Dronabinol, THC:CBD, THC	Unclear but some evidence against use
	Cannabis sativa	Unclear
	Nabilone	Unclear
Nausea and vomiting		
	Dronabinol	Low to moderate
	Nabilone	Very low to moderate
	THC	Low, insufficient evidence
	Levonantradol	Low to moderate
	THC:CBD	Insufficient evidence
	Cannabis sativa extract	Unclear
	Nabiximols	Insufficient evidence
Chronic non-cancer pain		
	Nabiximols	Moderate to high
	Dronabinol	Low to moderate
	Nabilone	Very low
	Cannabis sativa	Very low
	THC extract	Moderate
	THC:CBD extract	Low to moderate
	Ajulemic acid	Very low

Nabiximols is a TGA-registered medicine, under the tradename Sativex. It is a standardised extract of cannabis, containing roughly equal amounts of THC and CBD.

Dronabinol is a synthetic form of THC.

Nabilone is a cannabinoid synthesised in the laboratory, and has actions similar to THC although its chemical structure is different.

Ajulemic acid is a cannabinoid synthesised in the laboratory. It is similar to a breakdown product (metabolite) of THC but does not have psychoactive properties.



The side effects of medicinal cannabis treatment

Like all prescription medicines, medicinal cannabis products can have side effects. The extent of effects of these can vary with the type of medicinal cannabis product and between individuals. In general, the side effects of CBD-rich products are less than those for high-THC products, but because the required doses for CBD can be quite high in conditions such as paediatric epilepsies, a proportion of patients encounter side-effects with these CBD doses.

The known side-effects from medicinal cannabis treatment (both CBD and THC) include fatigue and sedation, vertigo, nausea and vomiting, fever, decreased or increased appetite, dry mouth, and diarrhoea.

THC (and products high in THC) have been associated with convulsions, feeling high or feeling dissatisfied, depression, confusion, hallucinations, paranoid delusions, psychosis, and cognitive distortion (having thoughts that are not true).



General cautions

- Patients should not drive or operate machinery while being treated with medicinal cannabis. In addition measurable concentrations of THC (tetrahydrocannabinol – the main psychoactive substance in cannabis) can be detected in urine many days after the last dose. It may take up to five days for 80 to 90 per cent of the dose to be excreted. Drug-driving is a criminal offence, and patients should discuss the implications for safe and legal driving with their doctor.
- Medicinal cannabis is not appropriate for:
 - people with an active or previous psychotic or active mood or anxiety disorder
 - women who are pregnant, planning to become pregnant or breastfeeding
 - people with unstable cardiovascular disease.
- Patients with neurological conditions may be more likely to experience negative effects from medicinal cannabis.
- There is no information available on the most effective or safe dose for various conditions and symptoms. For this reason, starting doses should be low and increased over time until patients respond positively or the negative effects outweigh the perceived benefits. Low start doses are particularly important for people with memory and thinking difficulties, liver and kidney disease, and weakness and wasting of the body due to severe chronic illness. Low start doses are also important for young people and the elderly.
- Doctors should:
 - carefully assess elderly and particularly sensitive patients
 - regularly monitor interactions between medicinal cannabis and other treatments.
 - assess liver function when deciding to continue or stop treatment.
- Although there may be some evidence to suggest a benefit from medicinal cannabis treatment for one condition or symptom, this does not mean it will have benefits for other conditions, even with the same product and the same dose.

There is very limited evidence to show how medicinal cannabis reacts with other approved medications.



More research is needed

There is a significant need for larger, high-quality studies to better explore the potential benefits, limitations and safety issues associated with medicinal cannabis treatment across a range of health conditions and symptoms.

More research will:

- increase the amount and quality of evidence to either support or contradict the use of medicinal cannabis as an approved treatment
- give a more detailed understanding of the most effective cannabis products, doses and administration methods for treating various conditions
- compare medicinal cannabis with standard first line medication options currently used to treat various conditions
- build a strong knowledge base on how medicinal cannabis interacts with other drug treatments.

Prescribing doctors should also collect data based on first-hand patient experience. This will further inform our knowledge and understanding of how to use medicinal cannabis effectively and safely.

As this new evidence emerges over time from doctors, clinical trials and other research, the Australian Government will progressively update the guidelines for both doctors and patients.



Further information

The TGA has developed more detailed clinical guidance documents for the use of medicinal cannabis products in treating:

- chemotherapy induced nausea and vomiting
- epilepsy
- multiple sclerosis
- pain
- palliative care.

You can find these documents and an overview guidance at www.tga.gov.au/...

The TGA website also includes more information on the use of medicinal cannabis products. Go to www.tga.gov.au/access-medicinal-cannabis-products

The Australian Government's Office of Drug Control provides useful information for cultivators, manufacturers, importers and exporters, and patients. Visit <https://www.odc.gov.au/medicinal-cannabis>

The United States' National Academies of Sciences has recently published a comprehensive review of the scientific evidence related to the health effects and potential therapeutic benefits of medicinal cannabis products. You can access "The Health Effects of Cannabis and Cannabinoids" at <https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state>



Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia

Email: info@tga.gov.au Phone: 1800 020 653

<https://www.tga.gov.au>

