# Clinical Guidance: for the use of medicinal cannabis products in Queensland

## March 2018

Queensland Government

# Contents

# Background

The following document provides guidance for Queensland health practitioners on the use of medicinal cannabis. As the evidence underpinning the clinical practice for use of medicinal cannabis evolves, it is anticipated, this document will be amended to reflect the current evidence.

The development of guidance documents at a national level was completed at the end of 2017 and these documents are available on the Commonwealth Therapeutic Goods Administration (TGA) website. The guidance documents were commissioned by the Commonwealth Department of Health and coordinated by the National Drug and Alcohol Research Centre (NDARC). They provide a review of the available evidence for the use of medicinal cannabis in palliative care, chemotherapy-induced nausea and vomiting, chronic non-cancer pain, multiple sclerosis and epilepsy. The guidance documents do not recommend medicinal cannabis use and do not fill the gap in research that currently exists, but provide medical practitioners who may choose to prescribe medicinal cannabis, under current access schemes, with some guidance as to the research available.

There is still substantial public interest in medicinal cannabis and, medical practitioners are likely to be asked to prescribe. However, as with all therapies medical practitioners must exercise their professional judgement in determining if this is an appropriate treatment for that individual patient. Medicinal cannabis should be considered only where conventional treatments have been tried and proven unsuccessful in managing the patient's symptoms. **It should be noted that medicinal cannabis is not considered a first line therapy for any indication**.

The following guidance is not meant to be comprehensive and should complement other reliable sources of information, including the national guidance documents. It may, however assist practitioners discussing medicinal cannabis use with patients.

This document should not be construed as endorsement from the Queensland Department of Health about the use, in individual patients, of medicinal cannabis products.

# Use of medicinal cannabis

Medicinal cannabis products in Queensland include products that are derived from the cannabis plant or synthetic products that act in the same way—and are used for a therapeutic purpose. Most presently available medicinal cannabis products are un-registered medicines (they have not been tested for safety and efficacy and approved by the TGA) and therefore their use in Queensland is only lawful under the *Public Health (Medicinal Cannabis) Act 2016* and subordinate regulations.

Research suggests that there may be some therapeutic benefit from the various cannabinoids contained within the cannabis plant. While research into the use of cannabinoids continues, the Queensland Government has enabled medical practitioners to access medicinal cannabis products for their patients before they have reached the standard required for a pharmaceutical product. This is only permitted if a

medical practitioner believes that medicinal cannabis may help relieve a patient's symptoms and/or medical condition.

To prescribe medicinal cannabis requires approval from both the State and the Commonwealth's Therapeutic Goods Administration (TGA). TGA approval is required for the supply and importation of the medicinal cannabis product and is through the TGA Special Access Scheme or Approved Prescriber Scheme, both of which allow access to unapproved therapeutic goods. The TGA cannot guarantee the safety, quality or efficacy of these products because they have not been through the rigorous TGA process required for medicine registration in Australia.

In addition, State approval is required to prescribe the product(s) to a patient, and, as with any other medication, the decision to prescribe should be made with knowledge of the risks, benefits, potential complications and drug interactions associated with the product. Medical practitioners should ensure they access available literature to determine the efficacy and safety of the product they wish to prescribe, to ensure they are comfortable with prescribing it. In addition, the *Public Health (Medicinal Cannabis) Act 2016*, commencing 1 March 2017, provides protection from civil liability when prescribing medicinal cannabis products provided the medical practitioner has acted in good faith and with due diligence. This protection may not extend to the TGA approval process.

Queensland Health recommends that medicinal cannabis that contains Tetrahydrocannabinol (THC) is generally not appropriate for patients who:

- have a personal history or strong family history of psychosis or have concurrent active mood or anxiety disorder
- are pregnant, planning on becoming pregnant, or breastfeeding
- have unstable cardiovascular disease.

The use of medicinal cannabis should be restricted to instances when the usual standard of care for the management of a patient's specified clinical condition and/or symptoms has been ineffective or produced intolerable side effects.

**It is not anticipated that medicinal cannabis products would be prescribed as first-line therapy at this time.**

**Note:**

There is one medicinal cannabis product, Nabiximols (Sativex®) which has been registered for use in Australia for the treatment of spasticity in multiple sclerosis patients. This medication has previously not been available but stock has now been secured for the Australian market. Within Queensland, use of this product is only lawful under the *Health (Drugs and Poisons) Regulation 1996* and is, at present, available for rehabilitation specialists and those specialists classified as patient class prescribers under the *Public Health (Medicinal Cannabis) Act 2016.* All other specialists and general practitioners need to apply to the Director-General Queensland Health for a Section 18 approval under the Health Drugs and Poisons Regulation 1996 (HDPR).

## Types of medicinal cannabis products in Queensland

- Flos/bud—Good Manufacturing Practice (GMP) certified cannabis buds or flower heads of known delta-9-tetrahydrocannabinol (THC)/Cannabidiol (CBD) percentage.

- Oils—varying combinations of THC and CBD.
- Liquid capsules—varying combinations of THC and CBD.
- Oro-mucosal spray—THC and CBD combination.
- Patches – CBD (usually only accessible in clinical trials)
- Gels - CBD (usually only accessible in clinical trials)

The Office of Drug Control website provides information on the medicinal cannabis wholesalers who have products available in Australia. Pharmacists are able to make contact with the wholesalers to determine cost of product and availability. The website can be accessed at:

https://www.odc.gov.au/importers-and-manufacturers-medicinal-cannabis-products

## Methods of administration

- Orally—oral-mucosal spray, sublingual oil or, orally ingested capsules or tablets.
- Vaporisation—using a vaporiser approved by the Therapeutic Goods Administration (TGA) as a medical device or until such a device is approved, devices approved in a similar jurisdiction.
- Trans-dermal application—patches or topical application of gel or cream.


The Volcano Medic and Mighty Medic which are approved medical devices in Canada.

**Smoking of medicinal cannabis products will not be approved in Queensland.**

# Cannabis

## Cannabis composition

There are approximately 500 natural components found within the *Cannabis sativa* plant, of which up to 100 have been classified as ‘cannabinoids’; chemicals unique to the plant. The cannabinoids are most abundant in the un-fertilised female flower head and this is the part of the plant utilised in the development of medicinal cannabis products.

The most well-known of the cannabinoids is delta-9-tetrahydrocannobinol (THC). It was isolated in 1964 in Israel. This cannabinoid is responsible for the psychoactive effects of cannabis and is the reason cannabis is used recreationally. However, it appears that 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 improvement in sleep and appetite.

A second cannabinoid, cannabidiol (CBD) is also showing promise in the medical field, but has the advantage of not being psychoactive. It appears that CBD may mitigate some of the THC effects and, while research is continuing, there is the possibility that CBD may be useful in the management of seizures, pain, and may have anxiolytic and antipsychotic effects. At this stage, it is not known if THC and CBD act individually or in conjunction with each other.

There are numerous other cannabinoids that may be of interest in the future, including cannabigerol (CBG), tetrahydrocannabivarin (THCV), cannabinol (CBN) and cannabichromene (CBC). Generally, all cannabinoids produced by the plant are in their acid form and in relatively low concentrations.

In addition to the cannabinoids, the cannabis plant also contains more than 400 other components. Of particular interest are the terpenoids or terpenes. These substances give cannabis its flavour and aroma and include terpenes such as myrcene, limonene and linalool.

Unlike the cannabinoids, terpenes are found abundantly in nature and particularly in many foods. Terpenes may also play a part in modulating the effects of THC when taken with cannabinoids, but may also have their own pharmacological effects. Many people who presently use cannabis as a medicine believe that the combined effects of the cannabinoids with the terpenes and the other components of the plant are what is required to achieve the desired ‘medical’ effect—this is commonly referred to as the ’entourage effect’.

The amount of cannabinoids (THC and CBD in particular) in a single cannabis plant varies considerably.  Different plants are gown to obtain specific ratios of THC to CBD that can then be used to manufacture different strengths of medicinal cannabis products.

Other cannabinoids

There are three groups of cannabinoids:

- Phytocannabinoids—derived from the cannabis plant as described in the cannabis composition section.
- Endocannabinoids—these are natural cannabinoids created by the body and which appear to exert a regulatory function within the body. Anandamide and 2-Arachidonoyl-glycerol (2-AG) are the two most studied endocannabinoids in the human body. They interact with the natural cannabinoid receptors found in the human body—CB1 and CB2.
- Synthetic cannabinoids—these are cannabinoids created in the laboratory. They include some pharmaceuticals such as nabilone (used for the treatment of anorexia and wasting in HIV/AIDS patients) but also other cannabinoids which are used recreationally, which are much more harmful, for example—HU-210 and JWH-018. Synthetic cannabinoids are not only full agonists at both CB1 and CB2 receptors, but they have 50 to 200 times increased affinity for the CB1 receptor compared with naturally occurring cannabinoids. This may potentially enhance the effects of these cannabinoids and increase the harms associated with them.

## The endocannabinoid system

The human endocannabinoid system was discovered in the 1990s and it appears to have a regulatory effect on many bodily functions. This cannabinoid signalling system is present in almost every life form, including the most primitive creatures.

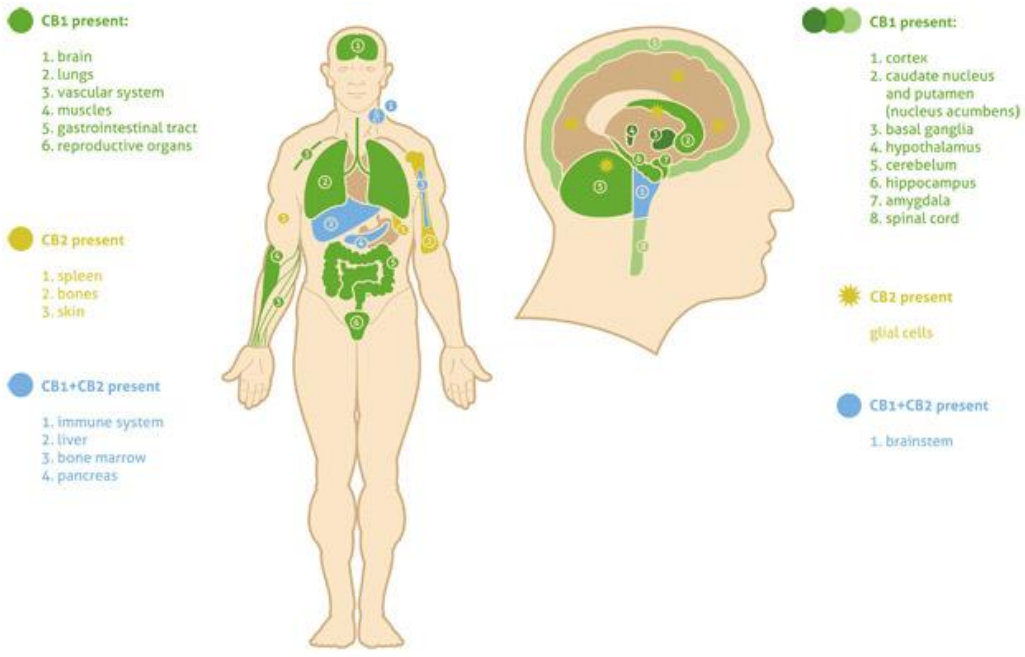
Multiple human and animal studies suggest that endocannabinoids play a key role in memory, mood, brain reward systems, drug addiction, and metabolic processes, such as lipolysis, glucose metabolism and energy balance.

Cannabinoid receptors are found all over the body but appear to be most prevalent in the following areas:

- CB1 receptors—highly concentrated in brain regions related to executive function, memory, cognition, mood, pain perception and movement. They are also found in the heart, intestines and bladder.
- CB2 receptors—found in the spleen, tonsils, thymus gland, bones, skin and the blood (monocytes, macrophages, B-cells and T-cells).

The endocannabinoids that interact with these receptors appear to be involved in the regulation of bodily functions, such as appetite, sleep, pain and inflammation, and may have a protective role in relation to brain function.

Cannabinoids found in the cannabis plant also interact with these receptors, in particular THC producing the euphoric effects most noticeable in recreational users.




Sites of CB1 and CB2 receptors (Source: https://www.fundacion-canna.es/en/endocannabinoid-system)

## Pharmacokinetics and pharmacodynamics of cannabinoids

Most data about the pharmacokinetics and pharmacodynamics is related to THC

- Smoking—smoked cannabis results in more rapid onset of action (usually within minutes), higher blood levels of THC and a shorter duration of effect. Peak levels are reached within 30 minutes and the effects may last for two to four hours. Smoking is the most common route of administration for recreational cannabis use but a person's physical response shows considerable individual variability because of the unknown concentration of THC in the products being consumed.

  At least 40 per cent of the THC dose in the cannabis is lost in side stream 'smoke'/combustion when smoked; making it difficult to estimate the amount of THC an individual patient is receiving. For this reason, and due to the well-documented evidence that smoking in general is harmful, smoking of cannabis products will not be approved in Queensland.
- Vaporising—vaporised cannabis results in similar rapid absorption and high blood levels as smoking it. Cannabis is heated at a lower temperature than smoking, producing fewer toxins and no side stream 'smoke', making passive smoking less of a problem. First effects occur within 90 seconds and reach a maximum after 15 to 30 minutes, before wearing off after two to four hours.

  Vaporising heats the cannabis without burning it and releases the cannabinoids and terpenes in the form of a vapour, which is then inhaled. Given the rapid onset of action, vaporising cannabis products is best for symptoms or conditions where rapid relief is required. The amounts of THC and other cannabinoids delivered by the vaporiser are dependent on the temperature, the duration of the vaporisation and the volume of the balloon in the vaporiser.

  **No vaporisers are presently registered in Australia as therapeutic goods.** The vaporisers shown above are registered as medical devices in Canada and Germany. If vaporised cannabis is to be used it is recommended that those which have been studied in a research setting and found to be safe and feasible are chosen for use.
- Oral route—medicinal cannabis products consumed in the oral form, such as oils or liquid capsules are more slowly absorbed. They take at least 30 to 90 minutes before any effects are felt. Bioavailability of oral cannabinoids is lower (10 to 20 per cent) because of intestinal and first pass liver metabolism. Peak effects can occur two to four hours after consumption.

  Given the longer time frame for peak effects, it is important to allow at least three hours between administration of single oral doses to avoid possible overdose. Effects can last for up to eight hours and as long as 24 hours. Given the slower onset and longer duration, it is expected that taking medicinal cannabis products this way would be more useful for medical conditions or symptoms where control over longer periods of time is sought—similar to the use of slow release medications.
- Oro-mucosal sprays—sprays appear to have similar mode of action as oral administration, as it is assumed that some of the product is swallowed. Effects typically start at about 90 minutes after administration and last about the same time

as orally administered cannabinoids. Titration of dose may be easier with oro-mucosal spray than with oral formulations.

- Topical — cannabis and THC are hydrophobic and are not absorbed through the skin. CBD and CBN are ten times more permeable than THC and are more likely to be used in topical preparations (patches and gels).

  The time of onset and duration of action are unknown. There have been some reports of hypersensitivity reactions, such as a rash and itching, when the skin has come into contact with medicinal cannabis products in this form.
- Acute toxicity of THC/CBD — medicinal cannabis products are generally regarded as having low acute toxicity, however, concurrent use of other drugs may mask the effects of cannabis and severe toxicity including adverse cardiovascular effects and death may be under-recognised. Although there have been no recorded deaths directly attributable to acute toxicity of cannabis in humans, in mammals the median lethal dose (THC) has been estimated to be >800mg /kg. CBD appears to be generally of very low toxicity. Doses of 1000mg/kg  CBD appear to have been tolerated safely in humans.
- Metabolism of cannabinoids — most cannabinoid metabolism occurs in the liver and involves the CYP450 pathway. THC accumulates in fatty tissue and is released slowly from this storage site. It is not clear if THC also persists in the brain.
- Excretion —THC and its metabolites are excreted through the faeces and the urine. It may take up to five days for 80 to 90 per cent of the total dose to be excreted; therefore THC is often found in the urine many days after ceasing use.

## Commencing treatment with medicinal cannabis

If medical cannabis products are being considered for a patient, it is essential that an accurate and thorough history is taken by the medical practitioner. This should include:

- presenting symptoms—the symptoms for which the medicinal cannabis product is being trialled to alleviate
- current medical history—in particular:
  - cardiovascular disease, liver disease and renal disease
  - conventional treatments that have been tried and have failed, as well as the length of time the treatments were trialled and the reasons for ceasing.
- past medical history
- psychological and psychiatric history
  - history of mental illness, particularly schizophrenia.
- risk behaviours associated with drug dependence. While previous /current cannabis use may not be a contraindication, care should be taken to manage the risk of dependence
  - nicotine dependence (may contribute to patient smoking product)
  - alcohol dependence/abuse
  - previous illicit drug use. (While previous use of illicit cannabis is not necessarily a contraindication, care should be taken to manage the risk of dependence).
- family health history

  - mental health, particularly a family history of psychotic illness
- social history
  - social support and family support for the use of a medicinal cannabis product
  - child safety considerations
  - employment, especially where it involves driving or operating machinery
  - risk of falls (in older patients or younger patients with mobility concerns)
  - family responsibilities such as caring for young children.
- physical examination
- investigations as needed
- medication review
  - other medications that might interact with medicinal cannabis
  - risk of side effects of medicinal cannabis products.

## The initial treatment plan

As stated above, a medical practitioner should complete a comprehensive clinical assessment of the patient that identifies risk factors that will need to be addressed before applying for access to medicinal cannabis. An initial treatment plan should indicate that the medicinal cannabis product will be used as a 4-12 week trial to determine the effectiveness of the medication for the patient's condition/symptoms.

The plan should clearly indicate:

- treatment goals for medical cannabis use—these need to be clearly documented and discussed with the patient, need to be related to the symptoms for which the patient is prescribed the medicinal cannabis and if possible, should be measurable. For example, weight gain in patients with anorexia and, cessation or minimisation of nausea and vomiting and improved function in patients with chronic non-cancer pain.
- if being managed by a general practitioner (GP), patient-specific supportive documentation for use of a particular medicinal cannabis product from a specialist in the field of medicine for which the symptom is being treated (e.g. palliative care) should be documented.
- risk management processes, such as frequency of dispensing. For example, weekly dispensing if there are concerns that a patient may self-escalate their dose.
- monitoring arrangements—weekly/fortnightly/monthly reviews, any blood tests, specialist reviews, other investigations (as needed) for the particular medical condition and/or symptoms being treated.
- an exit strategy for situations where the medication is not helping manage the symptoms or the goals of treatment are not reached.
- that informed consent has been obtained and the patient provided with information about the medicinal cannabis product, possible side effects and treatment goals, and that treatment will be discontinued if benefit has not been demonstrated.
- that the patient has been advised that they are not able to drive while on medicinal cannabis.

**The patient should sign and be given a copy of the plan with a copy filed in the patient's medical record**.

## Contraindications for medicinal cannabis treatment – products containing THC are generally not appropriate for patients who:

- Have a history of hypersensitivity to any cannabinoid or products used in manufacture (e.g. sesame oil).
- Have severe and unstable cardio-pulmonary disease (angina, peripheral vascular disease, cerebrovascular disease and arrhythmias) or risk factors for cardiovascular disease—THC acts through the CB1 receptors to decrease blood pressure, increase cardiac demand and causes vasodilation. In those who smoke cannabis, there is a four-fold risk of myocardial infarction in the hour following smoking in those patients with unstable ischaemic heart disease.
- Have a previous psychotic or concurrent active mood disorder or anxiety disorder.
- Are pregnant/breastfeeding—there are some reports of pre-term labour and low birth weight. Cannabinoids appear in the breast milk.

## Relative contraindications – while not preventing prescribing should also be considered by the medical practitioner

- Care should be taken in prescribing medicinal cannabis products containing THC to patients under 25 due to the potentially adverse effects on the developing brain. A risk analysis should be undertaken prior to prescribing these products.
- Severe liver or renal disease
- Drug dependence, including nicotine and heavy users of alcohol
- Other medications especially other sedatives such as opioids and benzodiazepines
- Paediatric and elderly patients—little is known about how these patient groups react to cannabis. As metabolism in the elderly is slower it is likely they will be more sensitive to the pharmacological effects of cannabis. Treatment should therefore be commenced at very low doses and adjusted very slowly.

# Therapeutic indications

**While there are many anecdotal reports of the therapeutic value of medicinal cannabis, the evidence to support the safety and efficacy of these products is limited**.

There has been strong consumer demand for medicinal cannabis products to be used more widely in the treatment of a number of medical conditions or for patients presenting with poor symptom control.

While animal data shows therapeutic potential and some human research has suggested some therapeutic potential, there is insufficient evidence by contemporary standards, such as randomised controlled trials, for most indications.

The national guidance documents provide information to support informed decision making and help patients partner with their doctor in determining if medicinal cannabis is a suitable option. The documents provide guidance for 5 therapeutic uses as well as an:

- **Overview** - https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-australia-overview.pdf and
- **Patient Information** - https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-australia-patient-information

The guidance documents include guidance in the following medical conditions:

- **Epilepsy** – adult and children - https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-treatment-epilepsy-paediatric-and-young-adult-patients-australia.pdf
- **Chemotherapy-induced nausea and vomiting** - https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-prevention-or-management-nausea-and-vomiting-australia.pdf
- **Multiple sclerosis** - https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-treatment-multiple-sclerosis-australia.pdf
- **Chronic pain** - https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-treatment-chronic-non-cancer-pain-australia.pdf
- **Palliative care** - https://www.tga.gov.au/sites/default/files/guidance-use-medicinal-cannabis-treatment-palliative-care-patients-australia.pdf

## Access Pathways for use of medicinal cannabis in Queensland

Queensland Health has provided for three pathways for medical practitioners to prescribe medicinal cannabis products containing THC, CBD or a combination of both.

Medical practitioners undertaking research in the use of medicinal cannabis are able to prescribe under the research protocol.

The **single-patient prescriber** pathway is available for any medical practitioner wishing to apply for a medicinal cannabis approval to treat a medical condition or symptom in an individual patient with medicinal cannabis. Single-patient prescribers will be required to provide evidence as to the safety and efficacy of the product they are requesting for use in that patient. It is anticipated that relevant and up-to-date clinical literature, including information provided in the national guidance documents, will be included with the application for the treatment of the patient to assist the Expert Advisory Panel in making a recommendation to the Director-General.

Medical practitioners who wish to prescribe for a patient with chronic non-cancer pain can do so under the single-patient pathway. It is suggested that the recommendations provided in the national document "*Guidance for the use of medicinal cannabis in the treatment of chronic-non-cancer pain in Australia, Version 1, December 2017*" form the basis of the application.

In the **patient-class prescriber** pathway Queensland Health has enabled the use of specific medicinal cannabis products by classes of specialist medical practitioners. Patient-class prescribers are limited to specialists in the relevant area of medicine and

are lawfully able to treat a group of patients with specific medical conditions/symptoms with specific medical cannabis products if they wish. These specialists will not have to apply for individual patient approvals in Queensland

Any medical practitioner seeking to prescribe medicinal cannabis products requires a relevant Commonwealth approval (Special Access Scheme or Authorised Prescriber) in addition to any legal requirements in Queensland.

The following specialists will be considered as patient-class prescribers at this time. The medicinal cannabis product types mentioned for each group are those that have been recommended in the national guidance documents.

| **Patient class prescribers** | |
|---|---|
| Paediatric neurologists and general paediatricians | Treating children with severe and drug resistant epilepsy with CBD products |
| Palliative care specialists | Treating patients with a terminal illness and symptoms such as loss of appetite, weight loss, cachexia with THC products; CBD products or THC: CBD combination products.<br>. |
| Neurologists | Treating patients with multiple sclerosis for pain or spasticity, with THC products or THC:CBD products<br>Treating young adult patients with epilepsy with CBD based products |
| Medical Oncologists (Paediatric or Adult)<br>(or other specialists providing chemotherapy) | Patients with intractable nausea and vomiting associated with chemotherapy or other cancer treatments can be treated with high THC products or THC: CBD products. |

## Dosing and administration

There are no precise dosing or established dosing schedules for products such as cannabis flos, vaporised oils, tablets or liquid (oil) capsules taken orally or for gels and patches used topically. Dosing is highly individualised and relies on titration of the product, regardless of the cannabinoid content, using the premise **'starting low and going slow'**. Finding the right dose, where therapeutic effect is maximised and adverse effects are minimised, requires patients and doctors to work together to determine the efficacy of the product for that patient and their medical condition.

Doses depend on the type of product used, individual variation, the development of tolerance, interaction with other drugs and previous exposure to cannabis either recreationally of medically. Lower doses are less likely to be associated with adverse effects.

Patients with no prior experience of cannabis who are initiating therapy for the first time are cautioned to begin with a very low dose, such as 1mg daily THC or lower, and to immediately cease the product if they have any side effects. This includes:

- disorientation
- dizziness
- loss of co-ordination
- agitation
- anxiety
- rapid heart rate
- low blood pressure
- hallucinations
- psychosis.

Doses should be increased slowly, preferably weekly, until a satisfactory dose is reached.

When initiating, therapy patients should be advised to have someone with them should they experience any adverse effects. All first doses should be given in the evening to assist with management of side effects.

Doses of THC as low as 2.5–3mg (and even lower), may be associated with a therapeutic benefit and minimal psychoactivity.

Average daily use in the Netherlands is approximately 650–820mg of vaporised cannabis. The THC consumption is then dependent on the strength of the cannabis product being used.

In the absence of studies using orally ingested oils, comparison with pharmaceutical products provides the best estimate of dosing levels. The available evidence for Marinol (oral capsule of synthetic THC dissolved in sesame oil) indicates an average daily dose of 20mg THC per day, with a maximum recommended dose of 40mg THC daily.

Nabilone (Cesamet) indicates a dosing range of 0.2mg–6mg per day.

Preliminary information from recent trials with Epidiolex (orally administered oil containing CBD) suggests a daily dosing range of 5–20mg/kg CBD (dosing in children). There is no known dosing range for adults.

Sativex, an oro-mucosal spray used for the treatment of spasticity associated with multiple sclerosis, recommends commencing treatment with one spray per day (2.7mg THC: 2.5mg CBD) and then titrating to a maximum of 12 sprays per day (maximum 32.4mg THC/30mg CBD daily). Sativex has also been used in a trial of cannabis withdrawal where it produced a short-term significant improvement in withdrawal symptoms when used for the first six days, but no change from placebo in THC use at one month.

**Patients should be commenced at the lowest possible dose especially in products containing THC, monitored carefully for adverse effects and increased slowly over days to weeks to determine if the product is effective.**

**Medical practitioners are encouraged to undertake pharmacovigilance and collect information on dosing levels especially in the older and younger age groups where there is little dosing information available.**

## Adverse events

A 2015 systematic review highlighted that there have been no studies evaluating the long-term adverse events of cannabinoids (Whiting et al, 2015). The research notes that further studies evaluating cannabis were required to improve the evidence of both the effects and the adverse events.

The authors concluded however, that cannabinoids were associated with an increased risk of short-term adverse events ranging from disorientation to psychosis. A summary estimate of adverse events with odds ratio for developing such an event in comparison to placebo or with active comparator was prepared and can be found at Appendix 2.

Any adverse event that requires alteration in the management of the patient, ceasing the medication, should be reported to the Therapeutic Goods Administration (TGA) and Queensland Health—see Appendix 1.

## Monitoring of patients

As these products are unapproved medicines, it is important that patients are reviewed regularly to ensure efficacy and to manage any adverse events. While no monitoring regimes are available internationally, it would seem appropriate that using a similar monitoring program to opioids would be clinically useful.

Patients should be reviewed more frequently when commencing on medicinal cannabis products, daily if needed. Once established on a dose, at a minimum monthly review is recommended.

Queensland medical practitioners prescribing medicinal cannabis are legally required to submit a report on the patient's progress if requested by the Director-General. This information will be used as a means of monitoring compliance with approval requirements, collecting information about the use of medicinal cannabis products in Queensland, hopefully informing further research into the area. It is anticipated that this information will be published and provided to medical colleges and networks to inform medical practitioners of the outcomes of medicinal cannabis use in Queensland.

At each review the medical practitioner should ensure the following areas are covered Symptom Control; Adverse events; Aberrant behaviour; Records (SAAR):

- symptom control—is the product improving the patient's symptoms?—For example, are they eating better, experiencing less nausea and vomiting, have improved pain management and spasticity or evidence of less seizures?
- adverse events—are they reporting any side effects? For example, is there any signs of drug-drug interactions that may require adjustment of the product or the other medications?
- aberrant behaviour— are there concerns that the patient may be on-selling their product? For example, are they using more than prescribed at any one time?
- records—it is important to keep adequate records, especially as this is an unapproved medicine.

### Transferring to another medicinal cannabis product

If another product is required, the treating medical practitioner should seek further approval from Queensland Health and the TGA. Approvals will, generally, be issued with a maximum daily dose of medicinal cannabis product(s) and for six or 12 months.

Any change in the product will require a new application for approval.

## Information for pharmacists and doctors (if supplying)

- Labelling—labels will be prepared in accordance with the *Public Health ( Medicinal Cannabis) Regulation 2017*
- Storage—medicinal cannabis products must be stored securely, as per the requirements of the *Standard for security of medicinal cannabis stock , January 2017*
- Some oil based products will require cold-chain management as well as to meet storage requirements as above.  Please contact the Medicinal Cannabis Unit for further information.
- Records—practitioners who obtain and store Medicinal cannabis products must record activity with the products as required under the Public Health (Medicinal Cannabis) Regulation 29017
- Disposal and destruction—any drug that is not dispensed or not used under the terms of the approval must be submitted to Forensic Scientific Services (FSS) for destruction (in the same way as the destruction of controlled drugs under the *Health (Drugs and Poisons) Regulation 1996)*.

  A completed Destruction of a controlled drug form must accompany all packages for destruction.
- Loss or theft of a medicinal cannabis product — prescribers and pharmacists are required to report discrepancies, losses or theft of these medicines to the Director-General, Queensland Health.
- Use the Department of Health notification form to notify the department of discrepancies, lost or stolen scheduled medicines. Email the completed form to MRQ@health.qld.gov.au

## Additional Information can be found at:

The following list is not exhaustive but will provide some information that may be useful for health professionals**.**

**It is highly recommended that medical practitioners wishing to prescribe medicinal cannabis undertake a search of the literature to establish the safety and efficacy of any products they are requesting to use.** This ensures they are able to provide the best possible care for patients when using an unapproved product.

- National Guidance on medicinal cannabis: Therapeutic Goods Administration, Australia

  https://www.tga.gov.au/medicinal-cannabis-guidance-documents

- Access to unapproved therapeutic goods: Therapeutic Goods Administration, Australia

  https://www.tga.gov.au/accessing-unapproved-products

- Cannabis Policy Framework: Centre for Addiction and Mental Health, Canada, October 2014

  https://www.camh.ca/en/hospital/about_camh/influencing_public_policy/documents/camhcannabispolicyframework.pdf

- Cannabinoids for Medical Use: A Systemic Review and Meta-analysis. Whiting et al. JAMA 2015; 313(24)2456-2473

  https://jamanetwork.com/searchresults?q=cannabinoids%20for%20medical%20use&f_JournalDisplayName=JAMA&SearchSourceType=3&exPrm_qgq={!payloadDisMaxQParser%20pf=Tags%20qf=Tags^0.0000001%20payloadFields=Tags%20bf=}%22cannabinoids%20for%20medical%20use%22

- Australian clinical trials information

  https://www.australianclinicaltrials.gov.au/

- Information for Health Care Professionals: Cannabis and the cannabinoids. Health Canada, 2013

  http://www.hc-sc.gc.ca/dhp-mps/marihuana/med/index-eng.php

- Cannabis: The Evidence for Medical Use, Michael Barnes and Jennifer Barnes, May 2016

  http://www.drugsandalcohol.ie/26086/1/Cannabis_medical_use_evidence.pdf

- Royal Australian College of General Practice: Medicinal use of cannabis products Position statement – October 2016

  http://www.racgp.org.au/download/Documents/Policies/Clinical/RACGP-position-on-medical-cannabis.pdf

- Faculty of Pain Medicine: Statement on “Medicinal Cannabis” with particular reference to its use in the management of patients with chronic non-cancer pain. 2015

  http://fpm.anzca.edu.au/documents/pm10-april-2015.pdf

- Victorian Law Reform Commission: Medicinal Cannabis Report August 2015

  http://lawreform.vic.gov.au/sites/default/files/VLRC_Medicinal_Cannabis_Report_web.pdf

- The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Report of the National Academies of Sciences

  https://www.nap.edu/download/24625

- Suite of Guidance documents from the Commonwealth Department of Health –

  https://www.tga.gov.au/access-medicinal-cannabis-products

## More information

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# Appendices

## Appendix 1—Adverse event reporting requirements

| Reporter | Reports what? | To whom? | In what format? | In what timeframe? |
|---|---|---|---|---|
| Treating doctor either in a hospital or in private practice | Any adverse drug | TGA | • TGA Blue Card<br>• Copy of Blue Card information to go to Queensland Health | As promptly as possible, to reach TGA within 15 days |
| | | Sponsor | As required by sponsor | As required by sponsor |
| | | Human Research Ethics Committee (HREC)* | As required by HREC | As required by HREC |

* If applicable, according to local rules for use of unapproved products within an institution and/or conditions imposed by HREC on its endorsement of the treating doctor.

https://www.tga.gov.au/publication/pharmacovigilance-responsibilities-medicine-sponsors

## Appendix 2—Leading adverse events, including odds ratio (adapted from Whiting et al, 2015)

| Adverse event | Odd ratio* |
|---|---|
| Disorientation | OR 5.41 |
| Dizziness | OR 5.09 |
| Euphoria | OR 4.08 |
| Confusion | OR 4.03 |
| Drowsiness | OR 3.68 |
| Dry mouth | OR 3.50 |
| Somnolence (drowsiness or sleepiness) | OR 2.83 |
| Balance problems | OR 2.62 |
| Hallucination | OR 2.19 |
| Nausea | OR 2.08 |
| Paranoia | OR 2.05 |
| Asthenia | OR 2.03 |
| Fatigue | OR 2.00 |
| Anxiety | OR 1.98 |
| Vomiting | OR 1.67 |
| Diarrhoea | OR 1.65 |
| Depression | OR 1.32 |
| Psychosis | OR 1.09 |

*The odds ratio is a measure of the increased (or decreased) chance of an event occurring compared to a comparator—in this case usually placebo.