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## Purpose

The Royal Australian and New Zealand College of Psychiatrists (RANZCP) has developed this memorandum to provide information for psychiatrists about the medicinal use of cannabis products, including in psychiatric practice. It is intended to provide information on the currently available evidence, guidelines and risks, particularly relating to mental disorder, to help inform psychiatrists who may be asked to prescribe it. The statement affirms the RANZCP's support for the further research and, where backed by sufficient evidence, appropriate regulation of medicinal cannabis.

### Key messages

- Although there is increasing public and medical interest in medicinal cannabis, the evidence upon which to base an assessment of the efficacy, effectiveness and safety of medicinal cannabis products is limited.
- Evidence for the use of medicinal cannabis in the treatment of mental disorders is very limited and there is no substantial evidence to support its use outside of properly approved research trials for these disorders.
- The RANZCP encourages further high-quality research regarding the use of medicinal cannabis for the treatment of mental disorders conducted under standard research trial conditions. If medicinal cannabis is being used outside of formal research trials then careful evaluation of this use is strongly encouraged.
- The prescription of medicinal cannabis for any condition should take into consideration the potential for misuse, dependence and side effects.
- Medicinal cannabis products should follow the same approval process as other new pharmaceuticals to ensure acceptable standards of effectiveness and safety are met before they are publicly accessible.

## Definitions and scope

*Cannabis* is the term given to products derived from elements of the cannabis plant used for medical or recreational purpose. Cannabis is known by a range of alternative terms (e.g. marijuana) but most medical producers and legislation use 'cannabis' as the preferred term.

*Medical cannabinoids* include a variety of chemical compounds, some synthetic and some extracted from the cannabis plant, which have been developed for medical use.

The cannabis plant contains many cannabinoids; the best known of which are delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD). (1) THC is the psychoactive part of cannabis that produces a 'high'. CBD has no psychoactive properties.

The terms medicinal cannabis and cannabinoids are used interchangeably when referring to the products derived from the cannabis plant for a medical purpose. This document predominantly uses the term medicinal cannabis, as that is the term used by both the Therapeutic Goods Administration (TGA) in Australia and the Ministry of Health in New Zealand.

This memorandum does not relate to the decriminalisation of cannabis for general cultivation or recreational use.

## **Background**

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There has been increasing interest in recent years in the use of cannabis for medical purposes. Governments at both Commonwealth and state and territory levels in Australia, and in New Zealand, have implemented legislative and policy change to allow the cultivation, manufacture, prescribing and dispensing of medicinal cannabis products in Australia (1) and New Zealand (2) for the management of medical conditions.

Medicinal cannabis has also been licensed for medical use in other countries including Canada, the United Kingdom and Germany, and some states in the USA. Given the public interest in medicinal cannabis, psychiatrists and other medical doctors are increasingly being asked to prescribe these products. Prescribing and use of medicinal cannabis requires careful consideration of relevant issues.

## **Evidence**

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- Although there is increasing public interest in medicinal cannabis, the evidence upon which to base an assessment of the efficacy, effectiveness and safety of medicinal cannabis products is limited.
- Recent reviews and analyses indicate there may be some therapeutic benefits of medicinal cannabis products in certain conditions (3, 4) although further research on their treatment efficacy and longer-term side effects are warranted. Most research and evidence on medicinal cannabis products have come from five clinical conditions: multiple sclerosis, palliative care, epilepsy, chemotherapy induced nausea and vomiting, and chronic non-cancer pain. (5)
- A recent systemic review and meta-analysis into medical cannabis for the treatment of mental disorders and symptoms of mental disorders reported that there is very little evidence to suggest that cannabinoids improve depressive disorders and symptoms, anxiety disorders, attention-deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder, or psychosis.(6) This study further found there to be very low quality evidence that pharmaceutical THC (with or without CBD) leads to a small improvement in symptoms of anxiety among individuals with other medical conditions. Evidence in the field of medicinal cannabis is nascent (7) and further high-quality studies directly examining the effect of cannabinoids on treating mental disorders are needed.
- It is important to note that evidence is based on the study of medicinal cannabis products. Any therapeutic potential of medicinal cannabis products will not necessarily extend to the cannabis plant itself. The use of illicit cannabis as a medication is difficult to evaluate due to the lack of standardisation of active cannabinoids and dose, as well as the conflation of medicinal use with recreational use, ingestion by smoking and risks of diversion. (8)

## **Risks and side effects**

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- There are no studies that have evaluated the long-term side effects of using medicinal cannabis products. (3) However, medicinal cannabis products are found to increase the risk of short-term adverse effects such as disorientation, dizziness, euphoria, confusion, among others. (5)

- Side effects from medicinal cannabis products generally depend on the amount of THC in the product. THC can impact on concentration and fine motor control, and have negative effects on driving ability or the use of machinery (9). Whilst THC blood levels associated with medicinal cannabis are often much lower than those associated with recreational cannabis use, the blood level associated with significant impairment is yet to be determined. The TGA recommends discussion between patient and doctor while under treatment with medicinal cannabis.
- Some population groups may be particularly vulnerable to adverse events resulting from the use of medicinal cannabis products. Risk factors include age, pregnancy, mental health status and cognitive capacity, and cardiovascular disease. (10)
- The TGA advises that medicinal cannabis is not appropriate for people with a previous history of psychosis, or concurrent active mood or anxiety disorder. Several studies have linked illicit cannabis use to increased risks for chronic psychosis. (11, 12)
- The risks of addiction associated with illicit cannabis use also suggest caution (13). However, studies looking at the side-effect profile of medicinal cannabis products suggest they are relatively well tolerated (14) and an initial review of by the World Health Organization's Expert Committee on Drug Dependence found no associated public health risks or abuse potential. (15)
- Its use in young people, particularly given the potential causal association between teenage use and later schizophrenia, urges particular caution. (9, 16) There is also evidence of potential negative impact – if used at high enough doses and for long enough - on certain aspects of neurocognitive functioning. (17)
- As with any medication, the side effects of specific medical cannabis products should be evaluated with the use of a risk–benefit analysis based on evidence of efficacy and safety. However, the relative paucity of firm data about efficacy and side effects in properly controlled trials which use specific combinations of particular cannabinoids for specific indications, make this challenging. (18). Medicinal cannabis doses should be individually determined, with maximum doses understood, and interactions with other medications considered. (7, 18)
- Manufacturer and supplier direct to practice 'education' is a potential issue. A lack of research, or the promulgation of misinformation by companies with a vested interest supplying medicinal cannabis products, may result in doctors making uninformed decisions that are not based on evidence or best practice and may compromise safety. Direct-to-consumer advertising for medications makes this a particular risk in New Zealand.
- Medicinal cannabis products are expensive as they are not subsidised by governments. The cost is prohibitive for many individuals, resulting in them, or their carer, turning to illicit sources of cannabis. (9)

## **Regulation of and access to medicinal cannabis**

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- Legislation in Australia and New Zealand only allows for the supply of medicinal cannabis products that are non-smokeable, medicinal-grade products, with Australia limiting supply to pharmaceutical grade products. At present, only one medicinal cannabis product (nabiximols) is approved for supply in Australia by the TGA and by Medsafe in New Zealand, as a treatment for multiple sclerosis. However, medicinal cannabis can be prescribed for other conditions in line with regulations. Given the developing evidence and political priorities in this area, regulations are subject to change. For example, in Australia, the TGA has confirmed that, from 1 February 2021, certain low dose cannabidiol products approved by the TGA and included on the Australian Register of Therapeutic Goods (ARTG) can be made available over the counter with pharmacist approval.

- In New Zealand, following an amendment to the Misuse of Drugs Act 1975 (Medicinal Cannabis Amendment Act in 2018), regulations came into effect on 1 April 2020 to establish a Medicinal Cannabis Scheme, administered by the Medicinal Cannabis Agency. Any medical doctor in New Zealand can prescribe unapproved medicinal cannabis products that meet the quality standard with no restrictions on the medical condition to be treated in line with prescription guidelines. (19) The need for specialist approval was removed as part of the introduction of these new regulations.
- In Australia access to prescribe medicinal cannabis products for 'off-label' conditions was opened up in 2017 through special TGA pathways for unapproved medicines, including the Special Access Scheme (SAS). This requires a specific form of medicinal cannabis to be specified for a particular indication in a particular individual, with a declaration that all other treatments have failed and with support from all the treating doctors. The alternative to the individual prescribing process is for a practitioner to become an 'authorised prescriber' of medicinal cannabis (which requires support of an ethics committee, as the RANZCP does not approve applications), or to develop an approved clinical trial. Each state and territory also has different laws governing access; the [National Prescribing Service](#) has developed resources.
- Pharmaceutical companies determine how they market their medicines, including whether to apply for approval to supply a prescription medicine. It is the view of the RANZCP that the regulation of medicinal cannabis products, where backed by sufficient evidence, should occur according to the same approval process as other new pharmaceuticals. The TGA in Australia and the New Zealand Medicines and Medical Devices Safety Authority (Medsafe) run well-established regulatory regimes which ensure that consumers have timely access to therapeutic advances with acceptable standards of effectiveness and safety, including consideration of the potential psychiatric implications for non-psychiatric conditions.

### **The use of medicinal cannabis by psychiatrists in practice**

- Psychiatrists should take the decision to prescribe carefully and cautiously taking into account evidence for safety, quality and efficacy, and after detailed discussions of the potential benefits and harms of medicinal cannabis products with the person to be treated.
- In Australia the TGA has developed a series of guidance documents to assist health professionals who choose to prescribe medicinal cannabis in Australia under current access schemes. In New Zealand Medicinal Cannabis Agency has set up a prescriber education program.
- It is anticipated that psychiatrists will most frequently be asked to prescribe medicinal cannabis as a potential treatment for a mental illness, or alternatively asked by other medical doctors for their advice on prescribing medicinal cannabis for conditions for which there may be, or potential for, comorbid physical and mental disorders. Psychiatrists are well placed to provide this advice as are very aware of the potential for misuse, dependence and side effects
- Based on currently available evidence, the use of medicinal cannabis for the treatment of psychiatric conditions is considered an innovative treatment. There remains insufficient evidence to provide guidance on the use of cannabinoids for treating mental disorders within a regulatory framework. (6) They should first be tested in randomised controlled trials and subjected to the same regulatory approval process as other prescription medications. (20)

The RANZCP therefore recommends that psychiatrists consider the following:

- It is preferred that the clinical use of medicinal cannabis, particularly for psychiatric disorders, should occur under robust clinical trials and case studies to test the efficacy, effectiveness and safety of long-term use of medicinal cannabis products, conducted under research trial conditions that include oversight by institutional research or clinical ethics committees with careful monitoring and reporting of outcomes.

- Psychiatrists who are considering the clinical use of medicinal cannabis outside of a research trial should:
  - be confident that medicinal cannabis is an appropriate option for the particular individual when other treatment options have failed
  - ensure that the patient is able and willing to consent to the treatment
  - ensure that clear information is provided to the patient, documented in the clinical notes, including an explanation that the use of medicinal cannabis is a novel treatment with detailed explanation of the current evidence and potential risks
  - discuss the treatment with peers (preferably including a second opinion from a psychiatrist or other medical specialist with experience and expertise in the use of medicinal cannabis)
  - ensure that medicines are accessed via appropriate processes in accordance with local laws
  - acknowledge the complexity of co-morbidities and potential for risk when prescribing off-label given the lack of evidence in this area may put people at greater risk of contraindications (21)
  - base their decisions on evidence, clinical indicators, and best practice ensuring that off-label use of medicinal cannabis has been subject to clinical trials to assure the efficacy, effectiveness and safety.
  - ensure the prescription of medicinal cannabis is subject to a regular review of progress, including monitoring for signs of aberrancy/diversion.
  - give due consideration to the medico-legal risks involved
  - where possible, seek institutional review by the medicines advisory committee or its equivalent
  - where possible, seek institutional research or clinical ethics committee consideration.

Where medicines containing cannabinoids are being prescribed 'off-label', see the RANZCP's [Professional Practice Guideline 4: 'Off-label' prescribing in psychiatry](#) for further information.

## **Research and education**

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- Legislation to enable the use of medicinal cannabis should be backed up by an ongoing commitment to fund high quality research. In Australia research is largely being funded through philanthropy and the growing number of private companies with an interest in producing medicinal cannabis products for commercial profit. (9) In New Zealand, whilst the Medicinal Cannabis Scheme intends to monitor prescriptions and any adverse effects experienced will be monitored, there is no coordinated approach to research.
- A priority is to make available high-quality medicinal cannabis products and develop a scientific evidence-base for their use. There is a need for comprehensive monitoring systems and tracking of outcomes associated with medicinal cannabis. This should comprise careful scrutiny of any adverse effects both at an individual level as well as more broadly in society as messaging that cannabis is 'safe and good for you' could potentially encourage use, with potential detrimental effects, notably amongst young people whose brains are still developing and in whom drugs such as cannabis can have negative effects on cognition and mood and (in those with a vulnerability) psychosis. (9, 16)
- Impartial education for the general public and medical practitioners should be made available. This education should reflect the current state of knowledge and contextualise the use of medical cannabis products as a last-resort medication for specific categories of illness that should only be prescribed in rare circumstances after stringent legislative criteria are satisfied. (5) Public education further needs to reinforce the distinction between medicinal cannabis

products and smokable and other illicit forms of cannabis, as well as between the different types of medicinal cannabis products available for use.

## Summary

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Further research is required to ascertain the potential risks and benefits of the targeted use of medicinal cannabis. Further high-quality studies directly examining the effect of medicinal cannabis on treating mental disorders are needed. There is a role for psychiatrists in contributing to this research, as well as supporting other medical colleagues in providing advice on potential risks in using medicinal cannabis for other medical conditions. The RANZCP supports legislation that facilitates the research and, where backed by sufficient evidence, appropriate regulation of medical cannabis. These products should follow the same approval process as other new pharmaceuticals to ensure these standards are met before they are accessible.

As the evidence for the use of medicinal cannabis continues to evolve, this memorandum will be reviewed and revised.

## Further reading

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National Prescribing Service (Australia). Information and resources for consumers and health professionals. [Available from: <https://www.nps.org.au/professionals/medicinal-cannabis-what-you-need-to-know>]

Royal College of Psychiatrists (UK). Position Statement on cannabis-based medicinal products. November 2019. [Available from: [https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/position-statements/ps05\\_19.pdf?sfvrsn=2db968d3\\_2](https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/position-statements/ps05_19.pdf?sfvrsn=2db968d3_2)]

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## Disclaimer

This information is intended to provide general guidance to practitioners, and should not be relied on as a substitute for proper assessment with respect to the merits of each case and the needs of the patient. The RANZCP endeavours to ensure that information is accurate and current at the time of preparation, but takes no responsibility for matters arising from changed circumstances, information or material that may have become subsequently available

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