

### Position

The Royal Australian College of General Practitioners (RACGP) highlights the need for further high-quality research into the safety and effectiveness of medicinal cannabis products, as the current evidence is limited and inconclusive.

The current available evidence does, however, suggest a possible role for medicinal cannabis products in a number of areas. Therefore, if after conventional, evidence-based treatments have failed, and the specialist general practitioner (GP) feels that medicinal cannabis products are a viable treatment option for their patients, they should, as other specialists can, be able to prescribe appropriate medicinal cannabis products in accordance with the current regulatory framework.

### Background

The February 2016 amendments<sup>1</sup> to the *Narcotic Drugs Act 1967*<sup>2</sup> allowed the supply of medicinal cannabis products for the management of patients with certain medical conditions. The amendments allow the supply of pharmaceutical, non-smokeable, medicinal-grade products. They do not include the provision of medicinal-grade herbal cannabis products and do not relate to the decriminalisation of cannabis for general cultivation or recreational use.

However, only one such product is currently registered in Australia. Therefore, most pharmaceutical grade medicinal cannabis products that are available overseas are not registered medicines in Australia, and approval from federal and/or state and territory authorities is required through the Therapeutic Goods Administration's (TGA's) Special Access Scheme or Authorised Prescriber Scheme. The RACGP has further developed a position statement on [The regulatory framework for medicinal use of cannabis products](#).

GPs are faced with the pressing need to help patients who are unable to manage chronic and debilitating conditions using conventional, evidence-based treatments. Given the significant media and political coverage on medicinal cannabis products, GPs may experience greater patient demand to prescribe these products. However, as with all clinical decisions, GPs need to balance patient initiated demands for treatment and the clinician's therapeutic responsibility, while considering federal and state or territory legislative requirements before considering the prescription of medicinal cannabis products. Refer to Appendix 1. Medicinal cannabis products checklist for more information.

This position statement does not recommend nor encourage the use of medicinal cannabis products; however, it recognises that as specialists, GPs may offer to prescribe medicinal cannabis products to a very limited number of patients with specific conditions in consultation with them and their care team. Importantly, medicinal cannabis products should only be considered when all first-line, conventional, evidence-based treatment options have been exhausted, and after detailed discussions of the potential benefits and harms of medicinal cannabis products with the patient.

The RACGP has always been a strong advocate for evidence-based medicine, and as the evidence around the efficacy and effectiveness of medicinal cannabis products evolve, this position statement will be reviewed to reflect the emerging evidence.

### Types of medicinal cannabis products

Cannabis is a complex plant comprising more than 500 constituents, including approximately 100 cannabinoids.<sup>3</sup> The main active ingredients used for medical purposes are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the psychoactive part of cannabis that produces a 'high', and has been used to treat symptoms such as nausea, pain and muscle spasticity. CBD has no psychoactive properties, and has been used to treat several inflammatory disorders and epilepsy.

Only pharmaceutical, non-smokeable, medicinal-grade products (listed in point one below) can now be supplied lawfully in Australia but medicinal cannabis products can come in three main forms:

1. **Pharmaceutical:** Natural and synthetic medical-grade products with standardised content. The three main products are:

- Dronabinol: Synthetic form of THC
  - Nabilone: Synthetic form of THC
  - Nabiximols: Chemically pure 50:50 mixture of TCH and CBD.
2. Medicinal-grade herbal cannabis: Produced and processed in controlled standard conditions to a medical grade, free of adulterants, higher levels of CBD and other cannabinoids, and contains lower levels of THC. This is provided in herbal form, or processed as an oil, balm, capsule or pill.
  3. Herbal cannabis on the illegal market: Potentially unstable THC and CBD, and may contain adulterants.

Currently, the only medicinal cannabis product registered for use in Australia is Nabiximols for the management of spasticity in patients with multiple sclerosis; however, this is not listed on the Pharmaceutical Benefits Scheme (PBS).

The cost of accessing medicinal cannabis products varies depending on the type and dose required, and the patient is responsible for all costs associated with this access. In several states and territories, patients may be eligible for medicinal cannabis products compassionate use schemes.

## Evidence base for medicinal cannabis

At present, the evidence base for the use of medicinal cannabis products is limited. The current evidence base for the use of medicinal cannabis products is heterogeneous, comprising a small number of randomised clinical trials when stratified by condition, symptom or intervention type. These studies are of variable quality, including those with high risk of bias (eg incomplete outcome data), low statistical power, and short follow-up time.

Recent reviews and analyses indicate there may be some therapeutic benefits of medicinal cannabis products in certain conditions;<sup>4,5,6</sup> however, further research on the treatment efficacy and longer term side effects are warranted.

Currently, most research and evidence on medicinal cannabis products have come from five clinical conditions – multiple sclerosis, palliative care, epilepsy, nausea and vomiting, and chronic non-cancer pain (refer to Table 1. Summary of evidence on medicinal cannabis products for more information). Numbers needed to treat and numbers needed to harm are included where possible.

### Multiple sclerosis

Around half the studies in a recent systematic reviews found that medicinal cannabis products may be effective for pain, spasticity, sleep and bladder function; the others were inconclusive.<sup>7</sup>

### Epilepsy

A number of studies have found low evidence for the use of medicinal cannabis products for the treatment of paediatric epilepsy, and for patients up to aged 25 years, especially when first-line treatments (ie anti-epileptic drugs) have been found to be ineffective.<sup>8</sup> The numbers needed to treat are as follows:

- 50% or greater reduction in seizure frequency: 8
- Complete seizure freedom: 171
- Improvement in parental-reported quality of life: 5

The numbers needed to harm for any adverse event was 3, and serious adverse event was 23.

### Palliative care

The use of medicinal cannabis products in palliative care is currently unclear.<sup>9</sup>

### Nausea and vomiting

A small number of studies have found relief of nausea and vomiting in patients with cancer who are undergoing chemotherapy; however, the evidence is lacking and some were compared with now out-of-date practices.

### Chronic non-cancer pain

There is some evidence available for the treatment of neuropathic pain using medicinal cannabis products; however, the magnitude of effect is small.<sup>10</sup> One systematic review found that the numbers needed to treat was 22 for a 30% reduction and 26 for a 50% reduction in self-reported pain intensity.<sup>5</sup>

**Table 1. Summary of evidence on medicinal cannabis products<sup>11</sup>**

Condition	Products	Quality of evidence <sup>12</sup>
<b>Multiple sclerosis<sup>7</sup></b>		
Pain	Dronabinol , THC extracts	Low to high and inconsistent
Disability and 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
<b>Epilepsy<sup>8</sup></b>		
Reduce by >50% and/or eliminate seizures	CBD with anti-epileptic drugs	Low to very low
	Oral cannabis extracts	Very low
	CBD:THC	Very low
	<i>Cannabis sativa</i>	Very low
Quality of life	CBD	Low
	Oral cannabis extracts	Very low
	CBD:THC	Very low
	<i>Cannabis sativa</i>	Very low
	THC	Very low
<b>Palliative care<sup>9</sup></b>		
AIDS	Dronabinol	Unclear
	<i>Cannabis sativa</i>	Unclear
Alzheimer's disease	Dronabinol	Unclear
Cancer symptom control	Dronabinol, THC:CBD, THC	Unclear, maybe against
	<i>Cannabis sativa</i>	Unclear
	Nabilone	Unclear
<b>Nausea and vomiting</b>		
	Dronabinol	Low to moderate
	Nabilone	Very low to moderate
	THC	Low, insufficient evidence
	Levonantradol	Low to moderate
	THC:CBD	Insufficient evidence
	<i>Cannabis sativa</i> extract	Unclear
	Nabiximols	Insufficient evidence
<b>Chronic non-cancer pain<sup>10</sup></b>		
	Nabiximols	Moderate to high
	Dronabinol	Low to moderate
	Nabilone	Very low
	<i>Cannabis sativa</i>	Very low
	THC extract	Moderate
	THC:CBD extract	Low to moderate
	Ajulemic acid	Very low
CBD, cannabidiol; THC, tetrahydrocannabinol		
Adapted with permission from Therapeutic Goods Administration. Guidance for the use of medicinal cannabis in Australia: Patient information. Canberra: TGA, 2017.		

## Adverse effects and drug interactions

A 2015 systematic review did not find any studies that evaluated the long-term side effects of using medicinal cannabis products.<sup>5</sup> However, medicinal cannabis products were found to increase the risk of short-term adverse effects such as disorientation, dizziness, euphoria, confusion, among others (refer to Table 2. Adverse effects of medicinal cannabis products for a full list). Side effects from medicinal cannabis products generally depend on the amount of THC in the product.

Recommendations from the Therapeutic Goods Administration (TGA) also highlight that THC is not appropriate for:<sup>13</sup>

- patients with a previous history of psychosis, or concurrent active mood or anxiety disorder<sup>14</sup>
- expectant mothers, female patients planning a pregnancy or those breastfeeding
- patients with an unstable cardiovascular disease.

Medicinal cannabis products are generally believed to have low acute toxicity; however, its concurrent use with other drugs may mask adverse effects such as cardiovascular effects, and mortality may be under-recognised.<sup>15</sup>

**Table 2. Adverse effects of medicinal cannabis products<sup>5</sup>**

Adverse effect	Odds ratio*
Disorientation	5.41
Dizziness	5.09
Euphoria	4.08
Confusion	4.03
Drowsiness	3.68
Dry mouth	3.50
Somnolence	2.83
Balance	2.62
Hallucination	2.19
Nausea	2.08
Paranoia	2.05
Asthenia	2.03
Fatigue	2.00
Anxiety	1.98
Vomiting	1.67
Diarrhoea	1.65
Depression	1.32
Psychosis	1.09

\*The odds ratio is a measure of the increased (or decreased) chance of an event occurring compared to a placebo

## Future developments

The RACGP recognises that while there are significant community and political interests in the medicinal use of cannabis products for therapy, the safety and effectiveness profiles of medicinal cannabis products are currently incomplete. The RACGP therefore highlights the need for further high-quality research into the safety and effectiveness on the use of medicinal cannabis products in Australia.

There is also a need to ensure that education for the general public and medical practitioners is 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.

## Appendix 1. Prescribing medicinal cannabis products checklist

Patient name:

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Patient address:

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Patient date of birth:

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As most medical cannabis products are not registered for use in Australia, special federal (ie Therapeutic Goods Administration [TGA]) and state/territory governments approval are needed to prescribe. This checklist aims to assist general practitioners (GPs) in that approval process.

### Part A. Before prescribing medicinal cannabis products

When considering whether medicinal cannabis products should be prescribed, it is important to have a detailed discussion of the potential benefits and harms of the treatment with the patient. All identified risk factors should be appropriately discussed, and ensure proper and accurate documentation. The following information should be documented in the patient's clinical notes, and points should be considered and discussed with the patient before prescribing medicinal cannabis products:

- Family history
  - History of mental illness, especially schizophrenia
- Past medical history
  - History of mental illness, especially schizophrenia
  - History of dependence of drugs of dependence
  - History of hypersensitivity to cannabinoid or products
- Current medical history
  - Cardiovascular, liver and renal diseases
  - Pregnancy and/or breastfeeding
- Physical examination
- Medication review
  - Potential side effects of medicinal cannabis products
  - Potential drug–drug interaction with concurrent medication
- Social support
  - Unable to drive while using medicinal cannabis products
  - Employment, especially in employment with machinery (eg forklifts, buggies) or high-risk occupations (eg at heights)
  - Risk of falls
  - Family responsibilities and support
- Clinical justification for the use of the medicinal cannabis products
  - Seriousness of condition and symptoms
  - All conventional, evidence-based treatment options that have failed
  - Length of time that the failed treatment options were trialled
  - Reasons for ceasing the treatment options that have failed
  - Safety and efficacy data to support the proposed use of the medicinal cannabis products (eg clinical trials, peer-reviewed articles)

### Part B. Treatment plan for medicinal cannabis products

TGA rules require a treatment plan to include a trial period (eg four weeks) to determine the effectiveness and efficacy of medicinal cannabis products for the patient, especially for symptom control. There is no precise dosing when a doctor chooses to prescribe medicinal cannabis products, as it is dependent on the patient's characteristics.

The following information should be documented in the patient's clinical notes, and points should be considered and discussed with the patient in the creation of a treatment plan for patients commencing medicinal cannabis products:

- Treatment goals
  - Ideally be measurable at proposed intervals (eg reduction in vomiting in patients with cancer who are undergoing chemotherapy)
- Documentation of support from the patient's other specialist(s) who is/are involved in their care (as required by jurisdictional legislation)
- Dispensing
  - Note: It is important to obtain the cooperation of the community pharmacist before you consider prescribing medicinal cannabis products. When applying for approval, you are required to nominate an eligible pharmacist to dispense the medicinal cannabis products. Only medicinal cannabis products for a specific patient is able to be held in an approved community pharmacy.
  - Frequency of dispensing
  - Location of dispensing
- Monitoring and review
  - Review of the treatment plan at proposed intervals
  - Additional investigations
- Ceasing treatment
  - Adverse effects are not tolerated
  - Medicinal cannabis products are not helping
  - Treatment goals are not reached
- Informed consent
  - Refer to Parts C–F

### Part C. Use of medicinal cannabis products

1. What are the clinical reasons for consideration for the use of medicinal cannabis products in this patient, include seriousness of condition and symptoms, and specialist recommendation:

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2. What are the treatment goals for the use of medicinal cannabis products, include trial period for review (Stop Rule):

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3. Past therapies that have been trialled and failed, include reason(s) and length of time:

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4. Outcomes and alternatives if medicinal cannabis products fails to achieve therapeutic goals and/or is ceased:

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5. Medicinal cannabis type, dose, frequency and route of administration, and location of dispensing:

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## Part D. Risks and side effects

### Unknown risks and late side effects

Medicinal cannabis products are still in an experimental phase of testing. There may be side effects and risks that are currently unknown. In the event that the use of medicinal cannabis products is ongoing, you will need to inform the patient/guardian of these risks and keep updated with any significant information regarding previously unknown risks. Possible side effects may include:

- Asthenia (abnormal physical weakness or lack of energy)
- Confusion, disorientation, dizziness, drowsiness, vertigo, sleepiness
- Balance problems, coordination
- Memory problems
- Diarrhoea
- Dry mouth
- Fatigue
- Hallucinations
- Vomiting or nausea

### Contraindications

Medicinal cannabis products are generally not appropriate for the following patients:

- Patients who have a history of hypersensitivity to any cannabis products
- Patients who have severe and unstable cardiopulmonary disease
- Patients who have risk factors for cardiovascular disease
- Patients who have a previous or current mental health condition
- Patients who are pregnant or breastfeeding

### Relative contraindications

Medicinal cannabis products should be carefully considered for the following patient:

- Patients who are aged 25 years or younger
- Severe liver disease
- Severe renal disease
- Misuse of drugs of dependence
- Interaction with other medications
- Paediatric and frail elderly patients with risk of falls

1. Potential risks associated with this specific patient, include family, and past and current medical histories:

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2. Potential interaction(s) with this specific patient, include social and medication reviews:

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3. Discussions, and questions and queries from the patient regarding medicinal cannabis products:

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## Part E. Patient declaration and consent

I understand that by taking medicinal cannabis products, I must:

- Attend regular reviews with my doctor and others healthcare providers (eg allied health professionals, other specialists) as advised by my doctor
- Undertake regular blood tests
- Follow my doctor's advice on dosage and frequency
- Report any adverse effects to my doctor
- Avoid the use of illicit and unprescribed drugs
- Avoid the use of alcohol
- Avoid driving or use of machinery
- Report the effects of the medicinal cannabis products to my doctor

I confirm that my doctor discussed with me information on the:

- Reasons why medicinal cannabis products may be used
- Treatment goals for the use of medicinal cannabis products
- Previous treatments that have been trialled and failed
- Outcomes and alternatives if medicinal cannabis products fail to have the desired effects and/or are ceased
- Type, dose, frequency and route of administration, and location of dispensing of the medicinal cannabis
- Risks associated with the use of medicinal cannabis products
- Potential interaction with the use of medicinal cannabis products
- Questions and queries I have about the use of medicinal cannabis products

I acknowledge that:

- There can be no guarantee that medicinal cannabis products will improve my/my child's condition
- Medicinal cannabis products are not registered for use in Australia, but an application will be made for access approval under the provisions of the relevant legal and medical frameworks in my state/territory
- I agree that I can withdraw my consent and ask that medicinal cannabis products be withdrawn at any stage with the assistance of my doctor

**Patient/parent/guardian (print):**

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**Patient/parent/guardian (signature):**

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**Date:**

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**Part F. Doctor declaration**

I declare I have personally discussed this form with the patient, including but not limited to, everything in parts A and B. I confirm that I gave the patient the opportunity to ask questions, which I have answered as fully as possible.

**Prescribing doctor (print):**

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**Prescribing doctor (signature):**

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**Prescriber number:**

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**Date:**

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## References

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- <sup>5</sup> Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: A systematic review and meta-analysis. *JAMA* 2015;313(24):2456–73.
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- <sup>11</sup> Therapeutic Goods Administration. Guidance for the use of medicinal cannabis in Australia: Patient information. Canberra: TGA, 2017.
- <sup>12</sup> Schünemann H, Brozek J, Guyatt G, Oxman A. GRADE handbook – Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. Hamilton, CA: GRADE Working Group, 2013.
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- <sup>14</sup> Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull* 2016;42(5):1262–69.
- <sup>15</sup> Dines AM, Wood DM, Galicia M, et al. Presentations to the emergency department following cannabis use – A multi-centre case series from ten European countries. *J Med Toxicol* 2015;11:415–21.