



Australian Government

Department of Health

Therapeutic Goods Administration



Guidance
for the use of
medicinal cannabis
in the treatment of
palliative care
patients
in Australia

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Table of contents

- Introduction.....1**
 - Review method 1
- Definition of palliative care2**
- Recommendations.....2**
- Caveats.....3**
- Efficacy.....4**
- Adverse effects.....4**
- Stopping rules.....4**
- NDARC Review 5**
 - Figure 1. PRISMA Chart..... 5
 - Identification..... 5
 - Screening..... 5
 - Eligibility 5
 - Included 5
- Overview 6**
 - Key to grades 6
 - Place in therapeutic hierarchy **6**
 - Treatment in specific disease settings 6
- Summary 10**
 - Route of administration..... 10
 - THC..... 10
 - THC:CBD 11
- Recommended duration of medication trial..... 11**
- Evidence of adverse events, drug–drug interactions, or patient groups for whom the product may pose particular risks relative to placebo..... 11**
 - Recommendation..... 11
- Appendix A..... 12**



NDARC Review	12
Use of tetrahydrocannabinol (THC)/cannabidiol (CBD) combinations or products	13
Table 1. Summary of included studies	14
References.....	15



Introduction

A set of guidance documents has been made available to assist doctors and their patients who choose to prescribe medicinal cannabis in Australia under current access schemes. These have been developed based on reviews of available evidence for the use of medicinal cannabis in five different settings. Included is an overview addressing the evidence base for medicinal cannabis therapy generally as well as specific documents relating to medicinal cannabis in the treatment of palliative care, epilepsy, chemotherapy-induced nausea and vomiting (CINV), multiple sclerosis (MS) and chronic pain.

This document reflects the evidence supporting the use of medicinal cannabis in palliative care patients and the recommendations of the Palliative Care Working Group.

Note: These guidance documents are based on evidence available at the time of publication and will be updated as new evidence emerges. Each document should be read in conjunction with the '*Guidance to the use of medicinal cannabis in Australia—Overview*'.

Review method

The Australian Government Department of Health commissioned a team from the University of New South Wales, University of Sydney and University of Queensland under the coordination of the National Drug and Alcohol Council (NDARC) to review the available evidence for the use of medicinal cannabis in the above five settings.

The researchers conducted a review of previously published reviews from multiple databases such as Medline, Embase, PsychINFO and EBM Reviews based on PRISMA⁷⁹. PRISMA is the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, and is an evidence-based minimum set of items for reporting on randomised controlled trials (RCTs). These guidelines have been developed because of concern for low quality trials and aim to improve the quality of medical research, remove bias and improve transparency and accurate reporting of findings. Searches were guided by a specialist Librarian using specific search terms and were limited to studies published between 1980 and early 2017. Two reviewers independently examined titles and abstracts for relevance using Covidence Software and the Cochrane Risk of Bias Tool was used to assess studies, aiming to increase accuracy. The GRADE (grading of recommendations, assessment, development and evaluation) approach, an internationally recognised standard applying to weighting of evidence in scientific and medical literature was used to evaluate the quality of evidence.

In July 2017, the department also convened five separate Working Groups to consider the available evidence for the use of medicinal cannabis in the treatment of each of the settings. The five groups consist of individuals from a wide range of backgrounds and organisations, including senior staff from each state and territory Department of Health, fifteen healthcare professional organisations, clinical staff from twenty-nine hospitals and healthcare systems, fourteen outpatient or Primary Health Networks and eighteen consumer representative groups.



Definition of palliative care

The World Health Organization's definition of palliative care is as follows¹:

'...an approach to care that improves the quality of life of patients (adults and children) and their families who are facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual. Palliative care also respects the choice of patients and helps their families to deal with practical issues, including coping with loss and grief throughout the illness and in case of bereavement.'

Palliative care provides relief from pain and other distressing symptoms. It:

- affirms life and regards dying as a normal process,
- intends neither to hasten nor postpone death,
- integrates the psychological and spiritual aspects of patient care,
- offers a support system to help patients live as actively as possible until death,
- offers a support system to help the family cope during the patient's illness and in their own bereavement,
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated,
- enhances quality of life, and may also positively influence the course of illness, and
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications².

Recommendations

Given the low number and generally poor quality of studies available to guide clinicians, it is recommended that patients be encouraged where possible to enrol in clinical trials of medicinal cannabis in palliative care. This document acknowledges that there will be times where trials of medicinal cannabis are not available but individual patients wish to be treated with these products. Under these circumstances it is strongly recommended that doctors emphasise the limited evidence for medicinal cannabis and the possibility of adverse events to the patient and their carers.

In the absence of evidence for first-line or sole use of cannabinoid products in palliative care, it is recommended that, should the treating physician elect to initiate medicinal cannabis therapy in palliative care patients, it be used after standard palliative treatments have been considered and used³. Australian guidelines for the management of symptoms in palliative care are available at <https://www.caresearch.com.au/caresearch/tabid/741/Default.aspx>.

Pharmacokinetic (PK) and pharmacodynamic (PD) interactions of medicinal cannabis products with chemotherapy and other medications are predicted but as yet not fully elicited.



Symptoms that may benefit are hard to define in the absence of evidence. Medicinal cannabis could be trialled to address ineffective treatment by other modalities for intractable symptoms, but stopped if adverse events occur or lack of benefit is demonstrated.

Oversight by the Therapeutic Goods Administration (TGA) of the standard of medicinal cannabis preparations, including the quality and quantity of cannabinoids supplied, is important to protect patients.

Recommendation

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.

Caveats

This document provides a guidance for health professionals in the use of an unapproved medicine, in the context of limited evidence of efficacy in end-of-life care.

While end-of-life care presents particularly emotive circumstances, quality and safety data for medicines are as important for people at the end of life, even though timeframes for an effective treatment with minimal harm is short. This vulnerable group of patients should not be put at higher risk by treatment with unproven products. This guidance addresses the tension between patient autonomy and the underlying therapeutic principle to 'do no harm' and intends to facilitate the patient's wish to try treatments to improve their quality of life.

The scope of the document is not specific to diagnosis or symptom cluster, but includes dosing suggestions for particular symptoms in terms of mixture of alkaloids and routes of administration.

In addition to the limited evidence for benefit of medicinal cannabis in end-of-life care, there are further caveats in this setting.

1. Guidance can only relate recommendations to the condition, drug and dose which have been studied. For example, evidence of efficacy in anorexia from one product and dose should not be extrapolated to pain control with the same product and dose.
2. There are limitations in how the evidence was obtained and reviewed.
3. Dose–response information for efficacy is lacking, in particular for starting doses. This is particularly relevant when applying data from younger people to the frail elderly or people with cachexia, cognitive impairment and hepatic or renal disease.
4. Dose–response information for toxicity of medicinal cannabis is also lacking, particularly for side effects which may overlap with symptoms of distress making appreciation difficult. It is also possible that side effects may occur at varying doses in this population and before efficacy is evident. Side effects which are reversible in younger people on ceasing the medicinal cannabis product may be irreversible in this setting.
5. There are no dose equivalence safety or efficacy data between specific medicinal cannabis products and current best practice (which may be best supportive care).



As with all therapies, medical practitioners must exercise their professional judgment in determining whether medicinal cannabis is an appropriate treatment for an individual patient. At this time, the use of medicinal cannabis should be considered only where other treatments have been tried and proven unsuccessful in managing the patient's symptoms.

Efficacy

The role of palliative care is much broader than prescription of therapeutic substances aimed at providing relief from pain and symptoms of illness. Studies of the use of medicinal cannabis in palliative care have addressed:

- as primary end points—impact on pain, body weight, appetite, caloric intake, nausea and vomiting, and
- as secondary end points—impacts on sleep disturbance, fatigue, mood, and health-related quality of life.

Although there are significant limitations of this data (unknown product constituents, route of administration and doses), there is some evidence of benefit of plant-based cannabis preparations in chronic neuropathic pain⁴ and in chemotherapy induced nausea and vomiting (CINV), but insufficient evidence to suggest benefit in advanced cancer patients with chronic pain unalleviated by optimised opioid therapy.

In patients without acquired immunodeficiency syndrome (AIDS), there is no evidence for weight gain or improved appetite and no evidence for improvement in mood. It should be noted that the modest benefit of medicinal cannabis products including dronabinol (a synthetic form of delta-9-tetrahydrocannabinol—THC) and nabilone (THC category) in CINV associated with moderately emetogenic anti-cancer drugs was demonstrated in comparison with prochlorperazine, which is no longer used in this setting. With severely emetogenic anti-cancer drugs, newer agents such as the 5HT₃ and neurokinin 1 receptor antagonists (palonosetron and aprepitant) appear more effective and better tolerated than medicinal cannabis.

A separate guidance document discusses CINV and the role of medicinal cannabis products in more detail.

Adverse effects

Details of adverse events with most medicinal cannabis products are lacking. However, sedation, nausea and dizziness are reported commonly. Serious adverse events have been described clinically, such as psychosis and cognitive distortion requiring external assistance, but the severity, time course and further details are not recorded.

Stopping rules

There is little information on dose–response. Starting doses should be low, and the dose increased in response to lack of efficacy until toxicity outweighs any benefit.

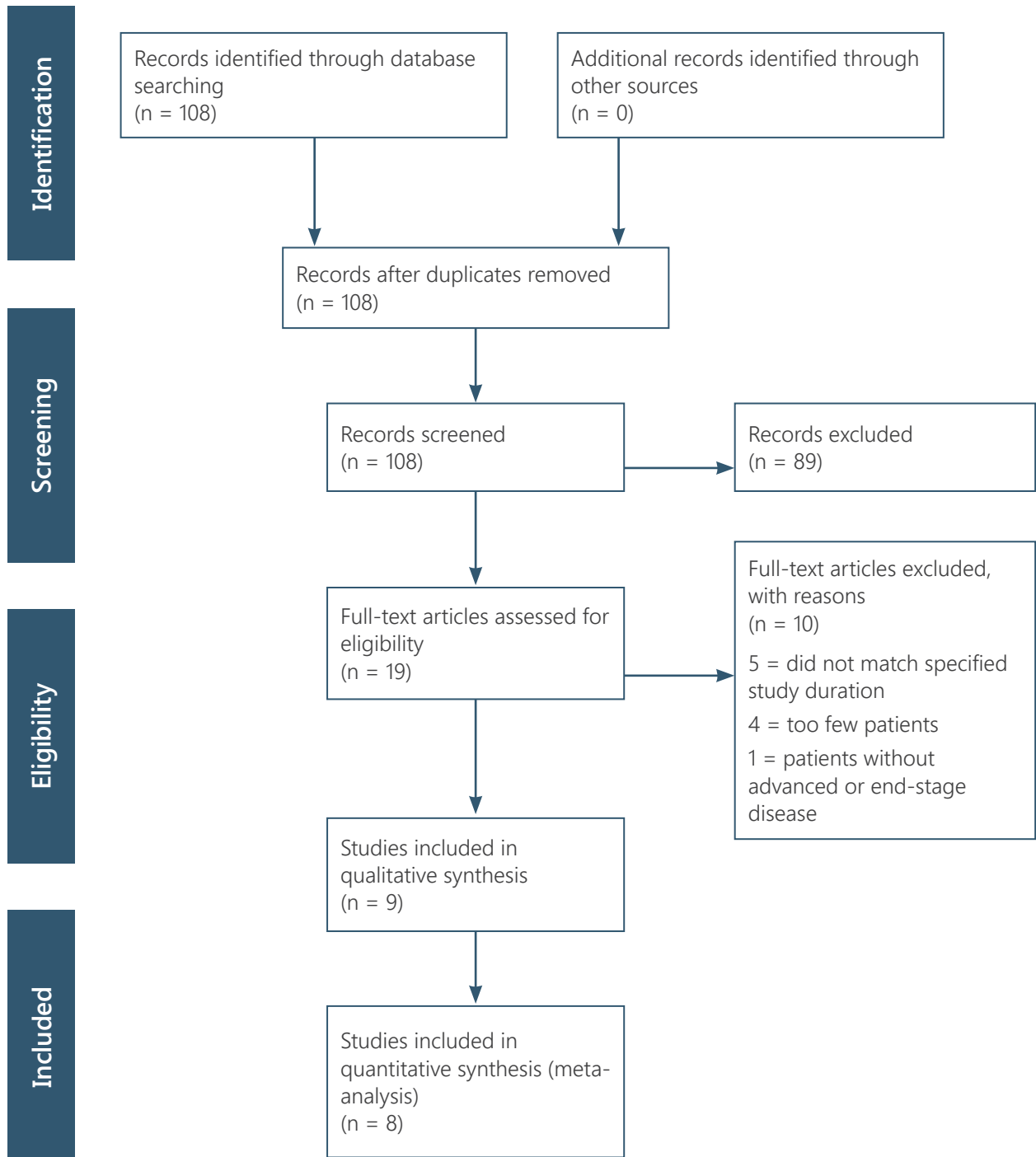
Information on pharmacovigilance should be collected by the prescribing doctor and pharmacist. This will help refine guidance documents and provide additional data.



NDARC Review

(See Appendix A)

Figure 1. PRISMA Chart



Overview

Key to grades

- A** Strong scientific evidence for this use
 - B** Good scientific evidence for this use
 - C** Unclear scientific evidence for this use
 - D** Fair scientific evidence against this use (it may not work)
 - F** Strong scientific evidence against this use (it likely does not work)
-

Place in therapeutic hierarchy

In studies of patients with cancer, medicinal cannabis products were used as adjunctive treatments. All patients continued treatment with radiotherapy or chemotherapy (noting that Johnson et al.⁵ excluded patients who had received radio- or chemotherapy in the last two weeks). The long-term use of opioids continued as usual⁶. Patients were excluded if they were receiving hormone therapies such as corticosteroids or other appetite stimulants. None of the studies or the reviewers of the studies drew any conclusions as to whether medicinal cannabis should be considered first-line or subsequent treatment in increasing appetite and weight. In one observational study⁷, morphine use decreased among patients who were receiving nabilone, compared to patients who continue treatment as usual. However this effect was not noted in other studies and does not provide strong evidence for the reduction of opiates once initiating medicinal cannabis therapy.

Medicinal cannabis has also been used as adjunctive treatments in patients receiving palliative treatment for HIV/AIDS. Patients continued to receive antiretroviral therapy (ART) or antibiotics while participating in these trials. Therapeutic hierarchy was not reported in these studies, and medicinal cannabis was assumed to be second-line treatment for symptoms such as appetite and weight gain to be used if megestrol acetate failed. It should be noted that current ART has significantly reduced AIDS-related morbidity and mortality and that the incidence of AIDS-related wasting has declined significantly.

Patients receiving palliative treatment for Alzheimer's disease continued their current medications. Therapeutic hierarchy was not reported in the studies, and medicinal cannabis was assumed to be second-line treatments used to increase caloric intake and improve negative affect.

Treatment in specific disease settings

Alzheimer's disease

Evidence

Dronabinol was dosed at 2.5mg twice a day in one study⁸. No significant differences were observed in comparison to placebo in decreasing pain, increasing caloric intake, or decreasing mood disorders.

One cross-over study with 15 patients provided low-quality evidence on the role of medicinal cannabis in the palliative treatment of Alzheimer's disease⁹.



Evidence Grade	Cannabinoid used	Outcomes
C	Dronabinol	Weight gain occurred in both treatment phases but patients who received cannabinoids before placebo gained more weight than patients who received placebo first.
C	Dronabinol	Negative affect decreased in both therapy phases but significantly greater reductions were observed when patients were receiving cannabinoids.

Tolerance and persistence in treatment

Evidence for the use of medicinal cannabis in patients with Alzheimer’s disease is from one cross-over study that included six weeks of placebo and six weeks of medicinal cannabis. A lack of efficacy, possibly due to the small sample size, meant that time to treatment response could not be assessed.

Outcomes

From the available evidence, outcomes that have been assessed in the palliative treatment of Alzheimer’s disease include:

- weight gain
- caloric intake
- mood disorders.

Overall there is limited evidence that these outcomes differed significantly between patients receiving medicinal cannabis and placebo.

Symptom Control in Cancer

Evidence

Five studies examined the use of medicinal cannabis for symptom control in patients with advanced cancer. Three studies were of moderate quality^{10,11,12}, and two of low quality^{13,14}. In a meta-analysis, there were no significant differences in outcomes between patients who received medicinal cannabis or placebo.

Evidence Grade	Cannabinoid used	Outcomes
C	Dronabinol, THC:CBD, THC	There was a non-significant effect of medicinal cannabis to reduce cancer pain.
D	Dronabinol, THC:CBD, THC	There were no significant differences between medicinal cannabis and placebo in effects on patients’ weight, caloric intake, appetite, nausea and vomiting, sleep, depressed mood, or quality of life. There were also no significant differences between medicinal cannabis and placebo in development of cognitive impairment or dizziness during treatment.



C	Cannabis sativa	All cancer and anti-cancer treatment symptoms (e.g. nausea, vomiting, mood disorders, fatigue, weight loss) were improved after initiating cannabis therapy. The lack of controlled studies restricts the conclusiveness of this finding and the clinical relevance is also unknown.
C	Dronabinol	Patients receiving dronabinol reported an increase in appetite and a decrease in nausea, however the treatment effects decreased as the disease progressed. The lack of controlled studies restricts the conclusiveness of this finding.
C	Nabilone	Patients receiving nabilone reported decreases in pain scores, morphine use, nausea, anxiety, overall distress, and borderline significant improvement in appetite. The lack of controlled studies restricts the conclusiveness of this finding.

When medicinal cannabis was compared with an active treatment (megestrol acetate), megestrol acetate was significantly better than the medicinal cannabis product in increasing patient appetite, weight, and quality of life.

After the literature review was conducted, two well-conducted, double-blind, randomised, placebo-controlled phase 3 studies of Sativex (THC:CBD) oromucosal spray as adjunctive therapy in advanced cancer patients with chronic pain refractory to optimum opioid therapy were published¹⁵. These did not demonstrate superiority of Sativex to placebo in reducing self-reported pain numerical rating scale scores.

Dosage

In one study, THC was delivered as an oromucosal spray, in which every 100µl spray contained 2.7mg of THC extract. Patients could administer up to eight sprays in any three hour period, with a maximum of 48 sprays in any 24 hour period¹⁶. In another study, THC was administered as an oral solution, dosed at 2.5mg twice per day¹⁷. The typical dose in the second study was far lower than in the first. Its effects were not significantly different from placebo on the measured outcomes of pain, appetite, nausea and vomiting, sleep disorders, mood disorders, and health-related quality of life. The Mayo Clinic reports that in order to increase appetite in people with cancer, 2.5mg of THC, with or without CBD, can be taken by mouth for six weeks¹⁸.

In two studies, dronabinol was administered at a dose of 2.5mg twice a day^{19,20}. In one study, the dose could be raised to 20mg/day. No significant differences were observed in comparisons with placebo in the measured outcomes of change in weight, increased caloric intake, increased appetite, nausea and vomiting, sleep disorders and health-related quality of life^{21,22,23}.

The Israeli clinical guide for medical clinical cannabis, based on advice from patients using these products but which is not based on trial data, recommends that for terminal or palliative care patients, CBD-rich flos, oil or cookies (for children) be used. The recommended product for starting treatment is 1 per cent THC: 10 per cent CBD, with the potential of moving to THC-rich products, such as 10 per cent THC:2 per cent CBD, up to 20 per cent THC:4 per cent CBD.



Tolerance and persistence in treatment

In the studies included in the review, treatment with medicinal cannabis products appeared to be tolerated well.

In studies of patients receiving palliative treatment for cancer, 16.2 per cent of patients dropped out due to adverse events such as somnolence, nausea and dizziness, compared to 14.5 per cent of patients who received placebo. There was no significant difference in the meta-analysis of dropout rates between medicinal cannabis and placebo.

In studies of patients receiving palliative treatment for HIV/AIDS, 7.6 per cent receiving medicinal cannabis dropped out of the study due to adverse events, compared to 3.4 per cent of patients who received placebo. There was no significant difference in the meta-analysis of dropout rates between medicinal cannabis and placebo.

One patient withdrew from the Alzheimer's study after experiencing a grand mal seizure after his/her first dose of dronabinol. Two other patients withdrew because of intercurrent infections.

Recommended review process for auditing patient outcomes, including suggested outcomes to evaluate

From the available evidence, outcomes that have been assessed in the effectiveness of medicinal cannabis in palliative cancer treatment include:

- minimum 30 per cent reduction in pain²⁴
- weight loss/gain
- caloric intake
- appetite
- nausea and vomiting
- sleep
- depressed mood
- quality of life
- cognitive impairment
- dizziness.

There is low quality evidence that medicinal cannabis produces clinically meaningful differences in the outcomes of appetite and weight gain. No difference between medicinal cannabis and placebo was observed on other outcomes.



Summary

Route of administration

Cannabinoid product	Condition	Preparation	Administration	Standardised
THC	Cancer	Oromucosal spray, capsule (herbal THC), capsule (as dronabinol), oil (as nabilone)	Oral	Dronabinol: yes Oromucosal spray and herbal capsule: Not specified Nabilone: Yes
	HIV	Herbal cigarette, capsule (as dronabinol)	Cigarette: Inhalation Capsule: Oral	Cigarette: No Dronabinol: Yes
	Alzheimer's disease	Capsule (as dronabinol)	Oral	Yes
	Spasticity	Capsule (as dronabinol)	Oral	Yes
THC:CBD	Cancer	Oromucosal spray, capsule	Oral	Not specified

THC

Herbal extracts of THC were delivered in the form of either an oromucosal spray²⁵ or in a gelatine capsule²⁶ taken orally. Information of standardisation of the products was not provided. Dronabinol is a synthetic form of delta 9 THC, and identical to purified natural THC. It is delivered as an oral capsule^{27,28,29,30,31}. It was approved by the Food and Drug Administration (FDA) for use in treating nausea and vomiting in the United States in 1985³².

In these studies, herbal cannabis was inhaled in the form of a marijuana cigarette³³. Dosage of THC was approximated according to the patient's weight but it was not a standardised dose or product. Medical cannabis supplier Tikun Olam Ltd. suggests that the general guidelines for smoking or vaporising cannabis are two or three inhalations, before waiting several minutes for the cannabis to take effect. However the variation in timing and depth of inhalations and effect on symptoms are unknown. It is recommended that inhalations are repeated until the desired dose is reached ("based on the feeling"). Oral products should be taken in small quantities, and patients should wait two hours to feel the effects of the active ingredients. This small ingestion and waiting for two hours is repeated until reaching the desired dose. Once the optimal dose is achieved, patients should wait six hours before taking another dose. Doses may increase slowly over a number of weeks³⁰.



THC:CBD

In other studies, THC:CBD was primarily delivered as an oromucosal spray in the form of nabiximols^{35,36}. In one study, the product was delivered in a gelatine capsule³⁷. Information on the standardisation of these products was not noted, although nabiximols are manufactured to GMP standard and approved for use in other indications (e.g. muscle spasticity for multiple sclerosis) in some countries (e.g. Australia, Canada, the European Union and the United Kingdom)³⁸.

CBD has not been used in the absence of THC in the palliative care setting.

Recommended duration of medication trial

There is little evidence based on the studies identified in the systematic review to inform decisions about treatment discontinuation. A reasonable rule of thumb may be that treatment should be discontinued if no benefits have been detected in any of these outcomes within the typical duration of these trials, i.e. four to 12 weeks.

Evidence of adverse events, drug–drug interactions, or patient groups for whom the product may pose particular risks relative to placebo

Based on the available studies, the most commonly reported adverse events in the use of medicinal cannabis products in the palliative care setting include:

- somnolence (20 per cent of patients)
- nausea (21 per cent of patients)
- dizziness (16 per cent of patients)
- confusion (10 per cent of patients)
- vomiting (11 per cent of patients)
- tiredness/fatigue (12 per cent of patients)
- anaemia (11 per cent of patients)
- pain (10 per cent of patients)
- asthenia (13 per cent of patients)
- diarrhoea (8 per cent of patients)
- headache (8 per cent of patients)
- dyspnea (8 per cent of patients)
- hallucinations (5 per cent of patients)
- in a small (15 patient) study, 11 had anxiety symptoms.

Recommendation

Patients and prescribing clinicians should be aware of possible adverse events such as somnolence, nausea and dizziness. Adverse events such as confusion, pain, diarrhoea or hallucinations may impact the overall aims of the palliative medicine and reduce quality of life, and should be evaluated on a case-by-case basis.



Appendix A

NDARC Review

Studies were assessed for their quality based on the criteria that the Cochrane Collaboration uses to evaluate possible methodological flaws in clinical trials³⁹. Overall, three of the nine studies were judged to be of moderate quality, and six were judged to have low methodological quality. Five studies had a high risk of attrition bias, one study had a high risk of performance bias, and one study was at high risk for selection bias.

Other concerns about the quality of the studies presented included their small sample sizes and a lack of follow-up on treatment. The small sample sizes meant that these studies were only powered to detect large therapeutic effects of a particular product. The lack of follow up reflects the challenges in evaluating the effectiveness of treatment in palliative care patients, many of whom are unable to complete the trial or clinical assessments because they are too unwell or pass away before the trial ended. In the absence of high quality controlled trials, with larger sample sizes, guidance for the clinical use of medicinal cannabis in palliative care must depend more on clinical judgment. With trials currently under way in New South Wales, this guidance may change in light of future findings.

An updated systematic review and meta-analysis of the available evidence on the safety and efficacy of using medicinal cannabis in palliative care treatment was conducted by NDARC in collaboration with Mücke and colleagues⁴⁰. Overall, the review found a small amount of evidence in one low-quality study⁴¹ to support the use of medicinal, cannabis to improve appetite, and in two low-quality studies^{42,43} to produce weight gain in patients with HIV/AIDS. It should be noted, however, that AIDS-related wasting is not now usually seen with the use of combination anti-retroviral therapy.

One low quality study⁴⁴ also reported that negative mood was significantly reduced when patients with HIV received medicinal cannabis rather than placebo in a cross-over study. There is no quality evidence to suggest that medicinal cannabis improves patient health-related quality of life or negative affect.

This study also found that active comparator, megestrol acetate was superior to medicinal cannabis in increasing appetite, producing patient weight, and improving quality of life in patients receiving palliative treatment for cancer (see Table 1).

The review included double-blind or open label randomised controlled trials (RCT) with parallel or cross-over design and a duration of \geq two weeks and \geq 10 patients per study arm. Each study required at least one of the primary outcomes to be addressed, defined on the basis of clinical experience:

Efficacy: Responder (pain reduction \geq 30%), body weight, appetite, caloric intake, nausea/vomiting (primary endpoints); sleeping dysfunction, fatigue, mood disorders, health-related quality of life, (secondary end points) at the end of each medication phase.

Tolerability: Number of patients, who discontinued the study due to adverse events, dizziness, mental illnesses and cognitive dysfunction.

Safety: Number of serious adverse events, deaths during treatment.



Non-randomised studies, short abstracts, case reports and studies without focus on palliative care were excluded from the initial systematic review search. For the purposes of the guidance review, an additional systematic search was carried out for observational studies, including retrospective chart reviews, prospective observational studies and case reports, regarding medicinal cannabis use in palliative care.

The review assessed risk of bias of each study using methodology recommended by the Cochrane Collaboration. These are:

- selection bias (randomisation, allocation concealment)
- performance bias
- detection bias
- attrition bias due to incomplete outcome data, and
- reporting bias⁴⁵.

Studies were defined as high quality if they had six to seven factors with low risk of bias, as moderate quality if they had three to five factors with low risk of bias, and as low quality if only zero to two factors of the seven were classified as low risk of bias.

After excluding duplicates, the literature search returned 108 publications. Eighty nine were excluded during screening of abstracts and nineteen full-text publications were reviewed. Ten studies did not match the inclusion criteria, five studies did not match the specified study duration^{46,47,48,49,50}, four had too few patients^{51,52,53,54} and one focused on patients without an advanced or end stage disease⁵⁵. In total, nine studies were included in the systematic analysis. These studies included five studies of patients with terminal cancer, three studies focused on palliative care in patients with AIDS, and one study of patients with late-stage Alzheimer's disease. An additional four observational studies were included for consideration when drafting the guidance document. Three studies focused on palliative care and symptom management in late-stage cancer, and one evaluated the effect of medicinal cannabis in treating spasticity in paediatric palliative care.

When the controlled studies were evaluated against the seven Cochrane criteria for possible methodical flaws⁵⁶, five studies were judged to be at high risk of attrition bias^{57,58,59,60,61}, one was at high risk of a performance bias⁶², and another one was at high risk of a selection bias⁶³. Overall, three of the studies were judged to be of moderate^{64,65,66} and six were judged to be of low methodological quality^{67,68,69,70,71,72}. All observational studies were judged to be of low methodological quality^{73,74,75,76}.

Use of tetrahydrocannabinol (THC)/cannabidiol (CBD) combinations or products

The published evidence has predominantly evaluated the efficacy of specific medicinal cannabis products. Five studies used synthetic THC preparations (but not specified as dronabinol), six used dronabinol (a synthetic form of THC), and three used a THC:CBD combination product.

One study compared the effectiveness of herbal cannabis to dronabinol⁷⁷ and found no significant differences in outcomes between the two. THC is one of the major psychoactive components in cannabinoids, and is largely responsible for stimulating appetite and eating and promoting relaxation. In comparison, CBD is believed to reduce convulsions, feelings of anxiety and psychotic symptoms⁷⁸. In palliative care, the effects of THC are likely to be more useful for patients because they help promote appetite.



Table 1. Summary of included studies

Condition	N studies	Cannabinoid used (N studies)	Outcomes studied	Effect	Quality of evidence
Cancer	8	THC (1)	Pain, appetite, nausea and vomiting, sleeping disorders, mood disorders, health-related quality of life	No effect	Low (N=5 studies)/ Moderate (N=3 studies)
		THC:CBD (3)	Pain, appetite, nausea and vomiting, sleeping disorders, mood disorders, health-related quality of life	No effect	
		Dronabinol (2)	Change in weight, caloric intake, appetite, nausea and vomiting, sleeping disorders, health-related quality of life	No effect	
		Cannabis sativa (1)	Change in nausea, vomiting, mood disorders, fatigue, weight loss, anorexia, constipation, sexual function, sleep disorders, itching, pain	No effect	
		Nabilone (1)	Pain, opioid use, nausea, anxiety, overall distress, appetite	No effect	
AIDS	3	Cannabis sativa (1)	Change in weight	No effect	Low (N=3 studies)
		Dronabinol (3)	Change in weight, appetite, nausea and vomiting, mood disorders, health-related quality of life	Dronabinol significantly increased weight and appetite, other outcomes not significant	
Alzheimer's Disease	1	Dronabinol (1)	Change in weight, caloric intake, mood disorders	No effect	Low (N=1 study)
Spasticity	1	Dronabinol (1)	Change in spasticity	No effect	Low (N=1 study)



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