



CIBG
Ministerie van Volksgezondheid,
Welzijn en Sport

Medicinal Cannabis

Information brochure for doctors and pharmacists

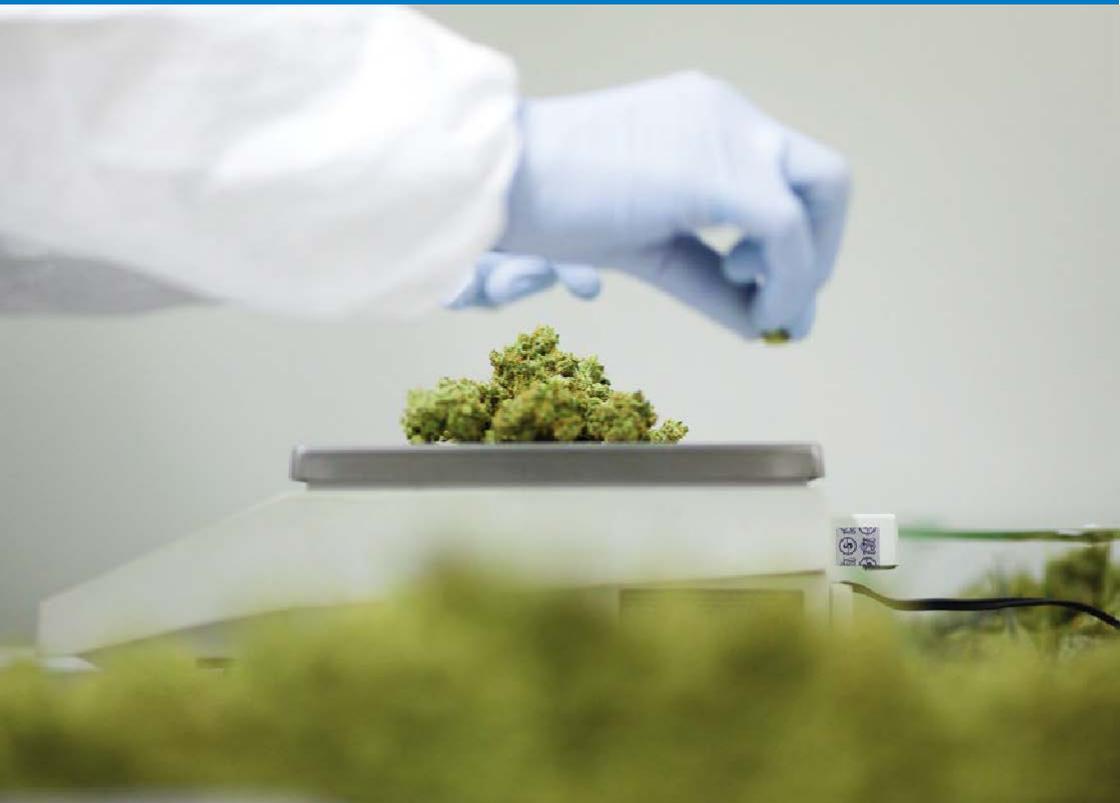


Table of Contents

Introduction	2
What is medicinal cannabis?	3
Application of medicinal cannabis	5
Dosage and use	8
Instructions for use and dosage	10
Adverse effects	12
Interactions and contra-indications	14
Medicinal cannabis abroad	15
Reimbursement	15
Cannabis online and on social media	16
Tips and areas for attention	17
Communication with your patient	18
Want to know more?	19

Introduction

Since September 2003, it has been possible for doctors to prescribe cannabis for medicinal use to patients, and pharmacists have been permitted to supply it on prescription. This has enabled medicinal cannabis to be used to treat medical symptoms under the supervision of a doctor and pharmacist. The supply and production of medicinal cannabis is the responsibility of the Office of Medicinal Cannabis (OMC).

Providing good support for patients who start using medicinal cannabis is important because of the different effects that the cannabis can have on each patient. The unusual way of administering medicinal cannabis and the fact that the dose must be adjusted based on the reduction of symptoms, and the occurrence of adverse effects, also make support essential. The most important issues you should discuss with your patients to ensure medicinal cannabis is used responsibly are listed under 'Communication with your patient'.

What is medicinal cannabis?

Medicinal cannabis, or more accurately Cannabis flos, consists of the dried flowers of the female Cannabis sativa L. plant (hemp plant). A distinction is made between the Cannabis sativa and Cannabis indica species. Cannabis contains a number of different active substances, including substances classed as cannabinoids, such as delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). The particular composition determines how the cannabis functions and what adverse effects may be caused. The medicinal cannabis obtained from a pharmacy is a standardised product that meets strict quality requirements. This cannabis is intended for therapeutic purposes, which is why we call it medicinal cannabis.

Available types of medicinal cannabis

The OMC supplies a variety of different types of cannabis. These differ in composition and strength and, therefore, in effect. Which type is suitable for which condition and which patient is determined by the doctor in consultation with the patient. You can ask the OMC for advice on the matter.

There are five types of medicinal cannabis available from pharmacies: Bedrocan®, Bedrobinol®, Bediol®, Bedica® and Bedrolite®, each with its own composition and strength (see table). Bedica® is the only product made of cannabis indica species: its different composition produces a different effect compared with e.g. Bedrobinol®. The type preferred depends on both the medical indication and the method of administration (see 'Applications per type').

Type	Dronabinol (THC) content	Cannabidiol (CBD) content
Bedrocan®	approx. 22%	<1%
Bedica®	approx. 14%	<1%
Bedrobinol®	approx. 13.5%	<1%
Bediol®	approx. 6.3%	approx. 8%
Bedrolite®	<1%	approx. 9%

Bedrocan® and Bedrobinol® are available as dried flower tops (flos). Bediol®, Bedrolite® and Bedica® have flowers which are ground up (granulate). Granulate is easier to dose and improves the ease of use for patients.

When used either with a vapouriser or to make tea, it does not matter whether the patient uses granulated or non-granulated medicinal cannabis.

Quality

The cannabis used by the OMC is grown under standardised conditions. This ensures that the medicinal cannabis has a consistent composition. Tests are performed to make sure there is no mould, bacteria, heavy metals or other undesirable additions in the cannabis. These quality requirements are documented in the ‘Cannabis flos’ monograph drafted by a certified company in cooperation with the OMC.

Application of medicinal cannabis

Cannabis receptors

A number of different cannabis receptors have been identified: CB1 and CB2 are the most well-known. The CB1 receptors are most commonly found in the central nervous system. Receptors of this type are chiefly responsible for pain modulation and the anti-emetic effect, but also affect memory and motor functions, among other things.

The CB2 receptors are chiefly located peripherally, particularly on immune system cells (chiefly in the spleen) and are, therefore, responsible for the immunological effects of cannabinoids. THC acts on both receptors.

Indications

There are scientific data available which suggest that medicinal cannabis may be effective for:

- Conditions with spasticity combined with pain (multiple sclerosis [MS], spinal cord injury);
- Chronic pain (particularly nerve pain);
- Nausea and vomiting (due to chemotherapy or radiation therapy in cancer, during HIV combination therapy and as a side effect of medication used to treat Hepatitis C infection);
- Palliative treatment for cancer and AIDS (to increase appetite and reduce pain, nausea and weight loss);
- Gilles de la Tourette syndrome;
- Therapy-resistant glaucoma;
- Epilepsy or epilepsy syndromes (including in children).

Experiences by patients and doctors also suggest that medical cannabis is clinically effective for conditions including Crohn's disease, ulcerative colitis, itching, migraine, rheumatic conditions, ADHD, PTSD, agitation in Alzheimer's disease and brain trauma. Efficacy has also been described for other conditions.

The website www.cannabis-med.org of the International Association for Cannabinoid Medicine (IACM) includes a database of scientific studies on cannabis and its therapeutic value in various conditions.

Medicinal cannabis produced by the OMC is not an authorised medicine. Treatment with medicinal cannabis may be considered if the usual treatments and authorised medicines are not effective enough or cause unacceptable adverse effects.

As far as we know, medicinal cannabis currently has no role to play in curing the aforementioned disorders, but it can reduce the symptoms they cause. Medicinal cannabis can also help reduce the dose and side-effects of other medication. It is up to the doctor to determine in what situation and for which conditions medicinal cannabis may be a suitable option for a patient. A doctor does not need to limit themselves to the list of conditions presented above.

Applications per type

Bediol® is a good first choice if the patient is inexperienced in the use of cannabis. The side effect profile is mild. If Bediol® proves insufficiently effective, a different variety containing a higher THC content may be considered. Different types may also be combined.

Cannabis which has higher levels of THC (Bedrocan®, Bedica® and Bedrobinol®) is most effective for symptoms such as poor appetite, weight loss and vomiting, anorexia, cachexia and emesis and for conditions such as Gilles de la Tourette syndrome and therapy-resistant glaucoma. When used as tea, these types can also have anti-inflammatory effects.

Cannabis containing CBD as well as THC (such as Bediol®) has proven effective for treating pain symptoms - with and without spasms - in patients with MS. This also applies to other conditions with spasms and abnormal muscle activity. CBD reduces the main adverse effects the THC might have and has anti-inflammatory properties. A product with CBD may, therefore, have a better effect on inflammatory conditions.

Bedica® – a cannabis indica variety – also has a strong relaxing effect on body and mind, in addition to the known effects of cannabis such as pain reduction. This may be a good choice for patients suffering from restlessness, insomnia or muscle spasms.

Bedrolite® contains less than 1% THC, and therefore has no psychoactive properties. There are indications that CBD may be effective in certain forms of epilepsy and epilepsy syndromes.



Dosage and use

The patient can use medicinal cannabis as tea or inhale it following vaporisation. Smoking cannabis is contraindicated because of its harmful health effects. Inhalation using a reliable vaporiser is a suitable method to administer it.

The active substances in cannabis are present as acids in the plant. Therefore, it is important for the patient to heat the cannabis before use (see 'Instructions for use and dosage') as this converts the acids into therapeutically active substances.

Usage

The method of use determines the absorption of cannabinoids in the body. The table below shows the important pharmacokinetic differences between a single dose of cannabis which is inhaled and one which is taken orally.

	Inhalation	Oral
Absorption	<5 minutes	30 to 90 minutes
Maximum effect	<15 minutes	after 2 to 3 hours
Duration of action	3 to 4 hours	4 to 8 hours

Achieving a 'steady state' situation and thus the maximum effect of repeated administration takes one to two weeks. We advise patients to take a fixed dose of cannabis every day at a fixed time.

The efficacy of the dosage used can be assessed by you as a doctor - together with your patient - after two weeks, and adjusted as necessary.

Dosage

The absorption of the active substances in cannabis, and hence the dose, varies strongly between individuals. When inhaled, this depends on - among other factors - the degree of heating of the cannabis, the inhalation technique, the number of inhalations, the waiting time between inhalations and lung capacity. When orally ingested as tea, the absorption is slow and variable.

The effect is slower than when inhaled. Eating fatty foods during oral ingestion can improve the absorption of the active ingredients.

As a doctor, you are responsible for determining the required amount and type of cannabis to be used per day. Start with a low dose to minimise the risk of (psychological) side effects. The dose can be increased gradually based on the patient's symptoms. There is no maximum dose. You can continue to increase the dose if the desired effect is not achieved, this means that the dose may vary between 1 cup of tea per week to several cups per day. For most patients, the effective dose will be lower than the dose at which any (psychological) adverse effects occur.



Instructions for use and dosage

As tea

- Bring 500 ml (0.5 litres) of water to the boil in a covered vessel.
- Add 0.5 gram (about 2 teaspoons or 1 measuring spoon) of medicinal cannabis.
- Turn down the heat and simmer the tea for 15 minutes with the lid on the pan.
- Remove the pan from the heat and strain the tea.
- Store the tea in a thermos if the patient wishes to drink more of it on the same day.

If the patient wishes to make tea for a few days in advance, we advise using 1 gram (about 4 teaspoons or 2 measuring spoons) of medicinal cannabis per litre of water. After preparation - as described above - the patient should add a sachet or teaspoon of coffee creamer powder to the warm tea. This prevents the active ingredients in the tea from sticking to the inside of the teapot or mug after cooling, which could reduce the efficacy of the tea. After cooling, the tea may be stored in the refrigerator for a number of days. If the patient wishes to use the refrigerated tea, it may be reheated. The patient can also add sugar, syrup or honey to improve the taste.

Dosage:

The patient usually begins by drinking 1 cup (0.2 litres) of tea in the evening. If the patient does not feel the effects are satisfactory after one to two weeks, they may - in consultation with you as a doctor - consume an additional cup (0.2 litres) of tea in the morning.

The use of tea is a good option to start with if the patient does not wish to inhale (yet). If the tea does not provide enough relief of symptoms, the patient may decide to inhale medicinal cannabis - in consultation with you as a physician.

Inhalation acts more rapidly and effectively than tea, and the correct dose is easier to determine.

Inhalation

Patients must use a reliable vaporiser or nebuliser for inhaling the medicinal cannabis. Nebulisers – with instructions for use – are available from the pharmacy where additional information on inhalation is also available. Alternatively more information can be found on our website www.cannabisbureau.nl.

Dosage:

- For initial use, place about 200 mg (1 teaspoon or half a measuring spoon) of medicinal cannabis in the vaporiser.
- Heat the cannabis and inhale once.
- Wait 5 to 15 minutes before the next inhalation.
- Repeat this a number of times, until the desired effect has been achieved or until (psychological) adverse effects occur. When first starting treatment, do this once or twice daily.
- It is important to increase the dose gradually, in consultation with the doctor. The cannabis dose can vary significantly between individual patients.

In practice, it has been found that patients can re-use medicinal cannabis that has previously been used in a vaporiser. Active substances are still released with reheating.

Smoking cannabis - both with and without tobacco - is not advised. We also do not advise using a bong/hookah as this also leads to the inhalation of harmful substances.

Oil

Medicinal cannabis is also available as an oil. There are various pharmacies in the Netherlands that manufacture oil from the medicinal cannabis produced by the OMC. This cannabis oil has a standardised composition. The patient uses it sublingually. Links to various pharmacies who prepare the oil may be found on **the OMC website**.

Adverse effects

Medicinal cannabis is generally well tolerated by patients. Adverse effects occur mainly at higher doses or if used in combination with a substance that enhances the adverse effects (such as alcohol). These adverse effects usually disappear within a few hours of use. Low doses of medicinal cannabis are often sufficient. Adverse effects are, therefore, relatively rare.

The use of medicinal cannabis can create psychologically adverse effects which can vary greatly and depend on the amount of cannabis, the method of use, the experience of the user and personal factors. Mood, for example, at the time of use, and the degree to which the patient is open to experiencing the effects, can both exert an influence. In rare cases, medicinal cannabis can trigger a psychotic reaction. This is characterised by delusions and hallucinations. There is a relationship between cannabis use and schizophrenia; a genetic predisposition appears to play a role in this.

At high doses, patients can become 'high'. This is a feeling of euphoria that slowly turns into a satisfied feeling of calm and tranquillity. Other possible side effects are relaxation, bursts of laughter, hunger, greater sensitivity to sensations such as colours and music, drowsiness and a distorted experience of time and space. Cannabis can also impair responsiveness. This is particularly common during the first two hours after inhalation, or the first four hours after ingestion.

An altered state of consciousness may evoke feelings of anxiety, panic and disorientation in patients. And, in patients who do not feel well before use, the negative mood may worsen. Restlessness and insomnia have also been reported.

Physical adverse effects of medicinal cannabis include tachycardia, orthostatic hypotension, headache, dizziness, sensations of heat and cold in hands and feet, redness, burning eyes, decreased muscle tone and dry mouth. Smoking cannabis can also lead to airway irritation.

Dependency

No information is known about whether there is any dependency associated with the therapeutic use of medicinal cannabis. Dependency is expected to be extremely uncommon if the cannabis is only used therapeutically. Caution is advised if there is a history of dependency.

Long-term use of high doses of medicinal cannabis can lead to dependency. Stopping treatment can then cause withdrawal symptoms, such as mild forms of restlessness, irritability, insomnia and nausea.

Overdose

Medicinal cannabis is not toxic, even at very high doses. An excessive dose may cause a low mood or anxiety, possibly leading to panic and fainting. Symptoms generally resolve themselves after a few hours. If necessary, doctors may administer a benzodiazepine (diazepam i.v.) in case of an overdose. In the event of tachycardia, treatment with a beta-blocker may be initiated (propranolol i.v.).



Interactions and contra-indications

Use of medicinal cannabis in combination with other substances which suppress the central nervous system - such as alcohol, benzodiazepines and opiates - strengthens the narcotic effect. Medicinal cannabis often has synergistic effects when added to existing therapies, which may mean that the dosage level of other medications - e.g. opiates, NSAIDs or benzodiazepines - can be reduced.

There is virtually no available research on cannabis' interactions with other medicines. THC is broken down by the liver enzymes CYP2C9 and CYP3A4. Theoretically, interactions can occur with drugs that strengthen or weaken the functioning of these enzymes.

Contraindications

Prescribing medicinal cannabis for patients with a predisposition for psychotic disorders or underlying mental disease should be done cautiously and its use should be properly supervised. If these patients benefit from medicinal cannabis, the use of a product containing CBD is preferred.

In patients with heart disease - such as cardiac arrhythmias and angina pectoris - the doctor should avoid prescribing higher doses of medicinal cannabis. This is because of the adverse effects on the heart (particularly tachycardia). Tolerance to these effects develops within days to weeks. This means the doctor should slowly increase the dose but be guided by any cardiac effects.

Research has shown that cannabis use can disrupt brain development in adolescents. Therefore, in adolescents (up to the age of 23 years), it is advisable to only use medicinal cannabis if the benefits significantly outweigh the risks.

Pregnancy and lactation

Use of cannabis during pregnancy and lactation is discouraged. THC can reach the foetus through the umbilical cord and pass into breastmilk.

Medicinal cannabis abroad

Medicinal cannabis is covered by the Opium Act. This means that doctors, pharmacists and patients must adhere to specific rules when prescribing, supplying and using medicinal cannabis. Rules pertaining to the use, and possession, of medicinal cannabis are different in the Netherlands compared to other countries. If your patient is travelling abroad and wants to take medicinal cannabis along, it is a good idea to organise this well in advance. More information on this topic is available on the CAK website, www.hetcak.nl

Reimbursement

Health insurance companies do not reimburse the costs of medicinal cannabis. If necessary, let patients contact their own health insurance companies to ask about reimbursement options.

Cannabis online and on social media

Use of cannabis for treating diseases and symptoms is popular. More and more people are buying CBD oil from chemists or online. Sales through other channels are also increasing. There are groups on Facebook and Instagram who buy and sell all kinds of different cannabis products, both dried and in oil form. The origin of these products is unknown and their production is not controlled. The quality of these products, what exactly they contain and in what quantity is unclear, and there are no guarantees that the production process is sufficiently clean.

The popularity of cannabis for diseases and symptoms also raises many questions online. Patients ask a lot of questions in discussion groups, on YouTube videos and on certain websites. The questions are often answered by people claiming to be experts, most of whom have no medical or pharmaceutical background. Recommendations are generally not based on scientific research. These websites often have a commercial interest, namely to sell as much cannabis as possible.

There are also stories circulating that cannabis can cure different types of cancers. Unfortunately, there is no evidence that cancer can be cured by cannabis at this time. Extensive research is being conducted worldwide on the effects that some of the components of cannabis may have on tumours. The results are currently limited. If your patients want to try using cannabis, it is important to discuss it openly with them. Make sure that patients do not see medicinal cannabis as a viable alternative to regular oncological treatments.

Tips and areas for attention

- An altered state of consciousness can cause confusion and anxiety in patients who use medicinal cannabis for the first time. You can advise your patients to use it for the first time in a familiar environment and in the presence of a friend or family member who can reassure them if necessary.
- Medicinal cannabis with a high THC concentration has a higher risk of causing psychologically adverse effects when inhaled. To reduce this risk, you may elect to use a variety with a low THC content at first (such as Bediol®) and then increase the dose gradually. You may also choose oral administration (tea). This method of administration is weaker. However, careful dosage is also required with tea.
- When adding medicinal cannabis to your patients existing medication, you may need to adjust your patient's medication. You can usually reduce the dose of other medication such as analgesics (including opiates) and spasmolytic medication while maintaining the same or better treatment effect.
- When inhaling medicinal cannabis, you must take the strength and composition of the cannabis into account. It has been found that inhalation of a double dose of a product with a low THC content does not have the same effect as inhaling a single dose of a product with a higher THC content. If you switch to a different product, you must also take the possibility of different efficacy into account.
- We do not recommend smoking. Smoke from medicinal cannabis combined with tobacco contains harmful combustion products. These health risks must be balanced against the severity of the condition being treated. Inhalation using a reliable vaporiser is a suitable and safe method of administration.
- The general assumption that use of a bong/hookah reduces the harmful effects of cannabis smoke is not true. Research has shown that the amount of harmful substances in the smoke decreases, but that the active substances - such as THC and CBD - are filtered out to an even greater degree. In the end, the patient

will have to inhale even more smoke to achieve a medicinal effect.

Communication with your patient

When prescribing and supplying medicinal cannabis, it is important for you as a doctor and pharmacist to provide the patient with good support. In any event you should ensure that you address the following subjects:

- The choice of the type of cannabis.
- The expected effects and the adverse effects.
- The recommendation to have a familiar person present for support during first use in case of anxiety or panic.
- Effects on reaction times.
- Strengthened narcotic effect of other medication.
- Storage instructions (in the original, closed container at 4-18 °C).
- Rules on taking medicinal cannabis on holiday.
- Reimbursement by health insurance companies.

In addition to the oral information provision, you can use written educational materials. The OMC and the Institute for Responsible Medication Use also have a joint information brochure available for patients which contains the information described above.

Want to know more?

If you have any questions, please contact the Office of Medicinal Cannabis (OMC) of the CIBG, Ministry of Health, Welfare and Sport, The Hague. The OMC is the national cannabis office. Our office is tasked with, among other things, (1) supplying medicinal cannabis, (2) ensuring the quality of medicinal cannabis and (3) providing information about it. The OMC works with a number of different partners in the Netherlands and maintains strong contacts with similar initiatives abroad. On the OMC website (**www.cannabisbureau.nl**) you will find answers to the most frequently asked questions about the medical use of cannabis.

On behalf of the OMC the Institute for Responsible Medication Use (IVM) has produced a publication on the theme of 'medicinal cannabis' containing information for care providers on supporting patients who (want to) use medicinal cannabis (**www.medicijngebruik.nl**).

Relevant websites

- Office of Medicinal Cannabis (OMC): **www.cannabisbureau.nl**
- Institute for Responsible Medication Use: **www.medicijngebruik.nl**
- CIBG, Ministry of Health, Welfare and Sport: **www.cibg.nl**
- KNMP Knowledge Bank: for more information, see **www.knmp.nl**
- International Association for Cannabinoids as Medicine: **www.cannabis-med.org**



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