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Schweizerische Gesellschaft für Cannabis in der Medizin
Swiss Society of Cannabis in Medicine
Société Suisse du Cannabis en Médecine
Società Svizzera di Cannabis nella Medicina

General information on the use of medical cannabis for professionals



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EFFECTS AND MECHANISMS OF ACTION OF THC AND CBD

The two main cannabinoids in cannabis that have been scientifically studied for medicinal application and are used in practice are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).

THC (also called dronabinol) has analgesic, anti-spasmodic, and appetite-stimulating effects, and is effective against nausea and vomiting. Moreover, THC can reduce intraocular pressure and improve sleep. In high doses, the substance has intoxicating or psychoactive effects; however, these effects are rare with oral therapeutic doses. THC elicits its diverse effects by binding to cannabinoid receptors in the endocannabinoid system, which is involved in the regulation of many different processes in the human body (pain processing, stress, appetite etc.).¹

CBD has anticonvulsant, anxiolytic, anti-inflammatory, and relaxing effects. Even in high doses, the substance does not elicit a “high” sensation. On the contrary, when used in combination with THC, CBD can reduce its psychoactive effects.^{2,3} The exact mechanism of action of CBD is not yet fully understood.¹

AREAS OF APPLICATION OF THC AND CBD



THC and CBD can be used for the symptomatic treatment of a wide range of diseases. The scientific evidence varies highly (see also *Therapy recommendations*).

THC

- Spasticity or muscle cramps; e.g. in multiple sclerosis, amyotrophic lateral sclerosis, paraplegia, cerebral palsy, Parkinson's disease, Alzheimer's disease, etc.
- Chronic pain; e.g. neuropathic pain, tumour pain, pain associated with polyarthritis, fibromyalgia, migraine, headache, etc.
- Nausea, vomiting, loss of appetite, and emaciation (e.g. in cancer patients)
- Neurological diseases; e.g. Tourette syndrome, restless legs syndrome, dyskinesias, etc.
- Glaucoma
- Sleep disorders

CBD

- Early-onset forms of epilepsy resistant to therapy (Dravet syndrome, Lennox-Gastaut syndrome)
- Anxiety and panic attacks
- Chronic inflammation and pain
- Muscular tension
- Depressive moods
- To alleviate drug withdrawal symptoms

The effectiveness of cannabis preparations is highly individual and dose dependent. The non-responder rate for cannabis preparations containing THC is approx. 30 %.

According to the current state of knowledge and the available literature, cannabis medication cannot be recommended as a first-line treatment. Every application should thus be considered an individual therapeutic trial if the guideline-compliant treatment is not effective or is not tolerated due to side effects.



MEDICINAL CANNABIS PREPARATIONS AVAILABLE IN SWITZERLAND

Various medical cannabis preparations are available in Switzerland, including oily solutions (or capsules) with pure THC (dronabinol) or CBD, as well as natural cannabis extracts in the form of tinctures and oils. These preparations are primarily intended for oral ingestion or local application in the oral cavity (Sativex® mouth spray).

Among the cannabis preparations currently available, two are registered by Swissmedic: Sativex®, authorised to treat spasticity in patients with multiple sclerosis, and Epidyolex®, authorised as an add-on treatment for seizures in children aged 2 and older with Dravet syndrome and Lennox-Gastaut syndrome (therapy-resistant epilepsies).

Furthermore, numerous extemporaneous preparations are available, produced by specialised pharmacies in Switzerland. These formulations vary in their composition (different ratios of THC to CBD concentrations) and their carrier material. A comprehensive list of all currently available preparations is available on the SGCM-SSCM website under *Therapy Recommendations*. The preparation best suited to an individual patient must be discussed with a health professional.

Please note that the aforementioned list only includes cannabis preparations authorised by Swissmedic and magistral preparations manufactured in compliance with GMP standards by a certified pharmacy. Freely available cannabis preparations are

not classified as medicines and cannot be prescribed. These products are not subject to any quality assurance or minimum content requirements, which does not allow for medical use at this time.

To obtain preparations containing THC, every patient requires a prescription for narcotics. An authorisation from the FOPH (federal office of public health) is no longer required since 1 August 2022. However, medical doctors are obliged to transmit details of the treatment to the FOPH via an online reporting system (www.gate.bag.admin.ch/mecanna). For cannabis preparations registered by Swissmedic and prescribed “on-label” (according to the authorised indication and dosage) (Sativex®), registration in the FOPH reporting system is optional. Pure CBD preparations (THC-free) can be prescribed with a normal medical prescription and are not subject to mandatory reporting to the FOPH.

For further information

- FOPH: “Change in the law on cannabis medicinal preparations” (in German, French and Italian only)
- Legal situation regarding CBD: see Swissmedic, FOPH, FSVO and FOAG “Products containing cannabidiol (CBD) – overview cannabidiol (CBD)”, version dated 21.04.2021 (fourth, updated version)



CONTRAINDICATIONS

Absolute contraindications for medicinal cannabis preparations are an allergy or hypersensitivity to cannabis, THC, CBD, or manufacturing-related accompanying substances (e.g. peanut oil in sativa oil 1%, or sesame oil in Epidyolex®).

For THC, a strict indication is moreover appropriate in patients with:

- serious cardiovascular diseases (coronary heart disease, cardiac arrhythmia, angina pectoris, myocardial infarction, etc.)
- serious psychiatric illnesses (in particular psychosis and panic attacks, also in medical history)
- current or previous addictive disorders
- children and young people aged under 18

The use of THC or CBD during pregnancy and breastfeeding is not recommended.

For registered preparations, the information for healthcare professionals must be consulted regarding contraindications, side effects etc.

VULNERABLE PATIENT GROUPS



Children and adolescents aged under 18 years

The benefit/risk ratio needs to be carefully considered before preparations containing THC are used for medicinal purposes in children and adolescents aged under 18 years. In principle, regular exposure of the developing brain to THC should be avoided as neurocognitive changes and/or permanent damage can be expected in the area of memory and attention. Similarly, structural changes may occur in the white and grey matter of the human brain, some of which persist despite subsequent abstinence.⁴ Only particularly serious paediatric diseases therefore justify the use of THC in this patient group.⁵

CBD is authorised in the form of Epidyolex[®] to treat two forms of childhood epilepsy (Dravet syndrome and Lennox-Gastaut syndrome) as an add-on therapy for children aged 2 or older. For other indications, as with THC, careful consideration of therapeutic potential/effect and the possible side effects is recommended.

Patients > 70 years of age and polymedicated patients

The use of THC and CBD in older patients is possible and very common in practice. In this patient group, it is advisable to set the initial oral dosage lower than usual (e.g. < 1 mg THC 2 to 3 times a day), followed by a slow increase, depending on clinical response and side effects. Special attention should be paid to the side effects of dizziness and drowsiness as they can lead to falls with potentially serious consequences.

In polymedicated patients, possible interactions with existing medications should be considered before starting a therapy (see section below on “Interactions with other medicines”). Moreover, it is advisable to start with a lower oral dosage than usual (e.g. < 1 mg THC p.o. 2 to 3 times daily), followed by a slow increase depending on clinical response and side effects.

DOSAGE OF THC AND CBD



THC

The optimal therapeutic dosage of THC must be determined individually. Dose finding can take two weeks or longer. It is important to start with a low oral dose, e.g. 2.5 mg THC or lower (e.g. for older and/or polymedicated patients), 2 or 3 times a day. The very first dose should preferably be taken in the evening. The dosage can then be gradually increased depending on tolerability until the desired effect is achieved. The motto is "Start low, go slow, stay low."

Depending on clinical response and tolerability, typical oral daily doses of THC usually vary between 2.5 mg and 30 mg THC (max. 50 mg THC/day, rarely higher), generally divided into several doses. The maximum single oral dose is 10 mg THC (rarely higher).

The effect of oral THC occurs after 30 to 90 minutes and lasts for 4 to 6 hours. In order to obtain a sufficient effect over the course of the day, several doses must therefore often be taken. However, depending on the symptoms, sporadic single doses may also be sufficient.

CBD

The dosage range for CBD is enormously large; oral doses of up to over 1000 mg CBD/day have been used in studies. In children with drug-resistant forms of epilepsy (e.g. Dravet syndrome, Lennox-Gastaut syndrome), oral doses between 2 and 5 mg, and sometimes up to 50 mg CBD/kg body weight/day have been administered in studies, divided into several doses.

For most other indications, evidence-based dosing recommendations are lacking. In practice, oral CBD doses of between 2.5 mg and 100 mg CBD/day are often prescribed (partly divided into several doses).



ADVERSE DRUG REACTIONS AND TOXICITY



In terms of side effects, a differentiation must be made between those of THC and those of CBD.

The potential side effects of THC include:

- Fatigue, sedation, drowsiness, dizziness
- Dry mouth, red eyes
- Tachycardia, hypotension
- Sickness, diarrhoea
- Headache
- Increased appetite
- Psychotropic effects (euphoria, dysphoria), cognitive impairment, impaired speech, hallucinations, depression, etc.

The potential side effects of CBD primarily include:

- Fatigue, drowsiness, sedation
- Reduced appetite
- (Reversible) increase in liver enzymes

Side effects are individual, mainly occur at the beginning of treatment, and are usually temporary. To prevent side effects, a slow titration of the dose is important, particularly for THC. If adverse reactions still occur, it should be determined individually whether the dose should be maintained, reduced, or if the therapy should be stopped.

Toxicity: Compared with certain other drugs, medicinal cannabis preparations have a low toxicity. Lethal doses in humans are not known so far.

Development of addiction: With correct medical use, the risk of developing addiction is extremely low.



INTERACTIONS WITH OTHER DRUGS

Medicinal cannabis preparations can usually be used in addition to existing medication. In some cases, however, dose adjustments may be necessary due to pharmacodynamic and/or pharmacokinetic interactions of cannabinoids with other drugs.⁶⁻⁸

Pharmacodynamic interactions

When combining THC and/or CBD with sedatives, hypnotics, opiates, alcohol, and other CNS-active drugs, an intensification of the effect (tiredness, sedation, drowsiness) is possible. Simultaneous use of THC and antihypertensives may lead to increased hypotension, particularly at the beginning of the therapy. Administration of sympathomimetic drugs and THC can lead to increased tachycardia. Combining anticholinergics with THC may cause increased mouth dryness, dry eyes, and a higher risk of confusion.

Caution is moreover advised when administering THC/CBD to patients under immunotherapy with checkpoint inhibitors (e.g. Nivolumab). Recently published research has indicated that cannabinoids may potentially weaken the effect of immunotherapy.⁹

Pharmacokinetic interactions

THC and CBD are metabolised in the liver by cytochrome P450 enzymes (CYP3A4, 2C9, 2C19 etc.). With simultaneous use of CYP inhibitors (e.g. ketoconazole) and CYP inducers (e.g. rifampicin, phenytoin), increased or decreased plasma levels of cannabinoids may occur.

CBD also appears to inhibit certain CYPs (e.g. CYP3A4, 2C9, 2C19).^{7,8} However, it has not been established at which CBD dose CYP inhibition occurs. Clinically relevant interactions have been reported for CBD and certain antiepileptic drugs (clobazam, rufinamide, topiramate).¹⁰ Similarly, significant interactions have been observed with warfarin¹¹, tamoxifen¹², and tacrolimus.¹³ Caution is therefore advised when administering CBD in combination with the following drugs:

- **Antiepileptic drugs:** clobazam, rufinamide, and topiramate
 - > increased plasma level of substances and/or active metabolites possible (N-desmethylclobazam)¹⁰
- **Tamoxifen:** decreased plasma level of the active metabolite endoxifen possible¹²
- **Tacrolimus:** increased plasma level possible¹³

- **Oral anticoagulants:** phenprocoumon, acenocoumarol
 - > increased plasma levels and consequently risk of bleeding possible
- Other CYP substrates with narrow therapeutic range

From practical experience, it can be reported that interactions of THC at therapeutic doses with concomitant medication seem to be clinically minimal or within the therapeutic window. In certain cases, however, dose adjustments may be necessary. In the case of CBD, interactions (e.g. with clobazam) have been observed in practice, especially at high doses. Clarification of possible interactions before starting the therapy is recommended in any case.

DRIVING



Basic information

In order to assess whether a motor vehicle driver is allowed to participate in road traffic, the two legal terms of ability to drive and fitness to drive should be understood.

Ability to drive refers to the momentary physical and mental ability of an individual to control a vehicle safely. **Fitness to drive**, on the other hand, refers to the non-temporal and non-event-related general mental, physical, and individual fitness of an individual to control a motor vehicle safely.

These two conditions (ability to drive and fitness to drive) must be met in anyone using public roads. The medical,

physical, and mental minimum requirements for drivers of motor vehicles are set out in Annex 1 of the Road Traffic Authorisation Ordinance.

Driving under the influence of cannabis

In Switzerland, driving a motor vehicle under the influence of cannabis (tetrahydrocannabinol, THC) is strictly forbidden (zero tolerance with an analytical limit of 1.5 µg/L = 1.5 ng/ml in the blood; Art. 2, para. 2, Traffic Regulations Ordinance, TRegO).

However, this “zero tolerance” policy does not apply if the preparations containing THC have been prescribed by a medical doctor (Art. 2 para. 2ter TRegO). If patients taking THC upon prescription

are involved in a police check or in a traffic accident, their ability to drive (i.e. their momentary ability to control a motor vehicle) will first be assessed. This assessment is carried out according to the three pillars principle (police observations, results of medical examination, results of forensic-toxicological analysis).

In case of reasonable doubts regarding fitness to drive, a corresponding assessment can subsequently be ordered in accordance with the Road Traffic Act. This assessment is performed by a medical doctor specialising in traffic medicine SGRM (level 4), taking into account all the relevant aspects, i.e. all present diseases, all prescribed medicines (in particular benzodiazepines, z-drugs, opiates etc.), addictive substance history, the THC blood concentration achieved under THC medication, cognitive abilities (potentially with an additional driving-related psychological assessment), etc. The person is not deemed fit to drive if there is a dependence on THC or on another psychotropic substance (Annex 1 RTAO). A history of abuse/dependence on illegal cannabis should – according to traffic medicine opinion – rule out a medical THC prescription.

If the assessments (in the case of a police check or traffic accident) on ability to drive and then on fitness to drive reveal that neither of these conditions are met, this will have consequences under criminal law, administrative law, and insurance law.

What should the prescribing doctor inform his patients about regarding traffic participation?

As part of their duty to inform, prescribing medical doctors should inform patients that THC medication can impair both their ability to drive and their fitness to drive.

Moreover, physicians can recommend that patients on stable THC medication undergo a fitness to drive assessment by a doctor specialising in traffic medicine. Please note that such an assessment cannot be performed by the attending medical doctor, only by a trained physician specialising in traffic medicine SGRM (level 4).

Registration by a physician for a medical assessment of fitness to drive is usually done with the patient's consent, but may be initiated without on the basis of the medical right to report in accordance with the RTA (however, there is no obligation to report on the part of the attending physician). Patients can also register themselves. The costs of a medical fitness to drive assessment (including a driving-related psychological assessment) must be borne by motor vehicle drivers themselves (approx. 2,500 Swiss Francs for a comprehensive assessment).

For patients with a driving licence in higher categories (bus, coach, truck, taxi, driving instructor, traffic expert), THC medication should in principle be avoided due to the generally much higher requirements for a licence.

Even if a patient on stable THC medication has been declared fit to drive, they must meet the conditions of ability to drive when participating in road traffic. Despite a confirmed fitness to drive, it may be possible that such an assessment is carried out again in some cases (e.g. due to changes to medication, dosage etc.).

Ultimately, every motor vehicle driver is himself/herself responsible for ensuring he/she is fit and able to drive before participating in road traffic. However, due to mutually reinforcing effects, patients taking a medication containing psycho-tropic preparations (including THC) should always abstain completely from alcohol when driving (0% blood alcohol content).

What is the situation with CBD regarding traffic participation?

When taking CBD on medical prescription, the same conditions apply regarding using public roads (the patient must be able and fit to drive).

In terms of CBD preparations, it should be noted that freely available CBD products may contain THC (in Switzerland legal if < 1% THC). As these preparations are not classified as medicines and cannot be prescribed, the zero tolerance rule is applied if THC is detected in the blood (see above).



COST COVERAGE BY THE HEALTH INSURANCE

Health insurance companies in Switzerland (both basic and supplementary insurance) are not obliged to cover the costs of a cannabis therapy (for the registered preparations Sativex® and Epidyolex®) or for the available magistral formulations. However, the attending physician can submit a request for cost approval to the insurance company. In some cases, health insurers will demand an initial self-financed therapy trial, cover the costs for a specific period, or contribute to the costs by paying a lump sum. A neutral cost approval request form for doctors can be found on the SGCM-SSCM website under *Therapy recommendations* and on the website of the *Swiss society of medical examiners and medical officers*. If there is no cost approval from the health insurance, the therapy costs must be covered by patients themselves.



FOREIGN TRAVEL

Every country has its own narcotics regulations. It is therefore important to contact the embassy or consulate of the destination country before taking medicinal cannabis abroad.

For journeys within the Schengen area, it is possible to obtain an official certificate from the physician to carry the Swissmedic-authorised product Sativex® (narcotic).

HOW TO OBTAIN MEDICINAL CANNABIS PRODUCTS



For cannabis preparations containing THC, the attending physician must issue a narcotic prescription for each patient. A FOPH authorisation no longer has to be applied for from 1 August 2022, as was the practice for many years. However, medical doctors are obliged to transmit details of the treatment to the FOPH via an online reporting system (www.gate.bag.admin.ch/mecanna).

For preparations containing only CBD (THC-free), a normal medical prescription is sufficient.

Please note that freely available cannabis preparations are not classified as medicines and cannot be prescribed. These products are not subject to any quality assurance or minimum content requirements, which does not allow for medical use at this time.

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