

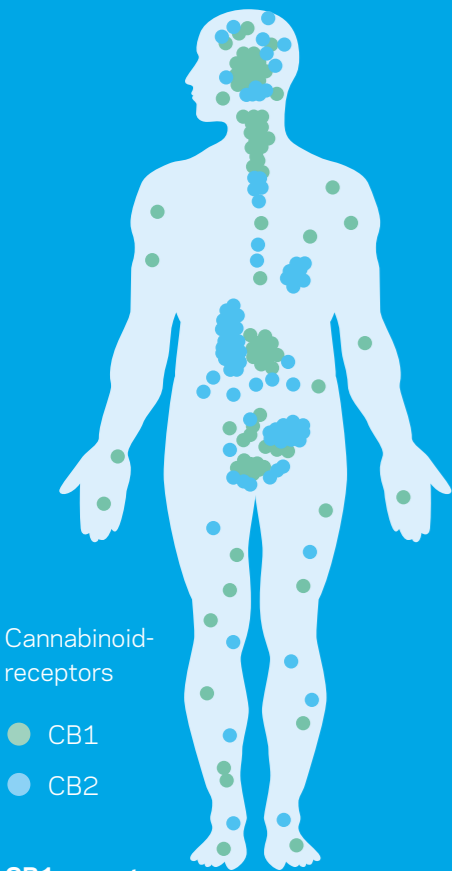


AURORA[®]



Cannabis Flower

Information for Health Care Practitioners



Cannabinoid-receptors

- CB1
- CB2

CB1 receptor

CB1 receptors are one of the most common G-protein receptors in the brain and the CNS.

Effects:

- pain modulation
- memory formation
- appetite regulation
- regulation of body temperature
- movement control
- information processing
- cognitive control
- emotional processing

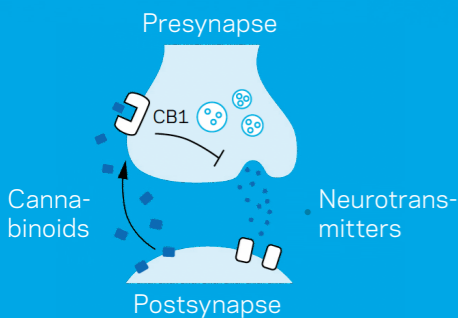
CB2 receptor

CB2 receptors are located mainly in immune cells and peripheral tissue.

Effects:

- immune response
- cell migration
- release of cytokines

Signalling at the synapse



The Cannabis Plant

The cannabis plant contains over 100 different phytocannabinoids, the main therapeutic agents being dronabinol THC and CBD. The flower of most varieties predominantly contains THC, which is responsible for the psychotropic effects of cannabis.

In the cannabis flower, the cannabinoids THC and CBD are mainly present in the form of their respective acids, THCA and CBDA.¹ Only by decarboxylation, which is achieved by heating the plant material, do the effective molecules THC and CBD arise. With full extract cannabis oils, decarboxylation takes place during the manufacturing process so the cannabinoids present in the final product are available in their active forms.² Cannabinoids bind to the body's own CB1 and CB2 receptors and have the potential to reduce overactivity in neurotransmitters.³

Endocannabinoid System

The endocannabinoid system is part of the nervous system and includes ECS signalling molecules (anandamide and 2-arachidonoylglycerol [2-AG]) and cannabinoid receptors (CB1 and CB2 receptors) with their natural ligands – the endocannabinoids.

CB1 and CB2 modulate different ionic channels and affect cell signalling pathways. While CB1 is associated with the modulation of learning and movement processes, CB2 is thought to have a regulatory effect on the immune system. Other physiological processes involving the endocannabinoid system include pain regulation. The effects of endocannabinoids occur via a retrograde mechanism in which endocannabinoids are released by postsynaptic neurons into the synaptic cleft and act in a retrograde manner at the presynaptic neuron. This temporarily or permanently inhibits the neurotransmitter's effects at the affected excitatory or inhibitory synapse.⁴

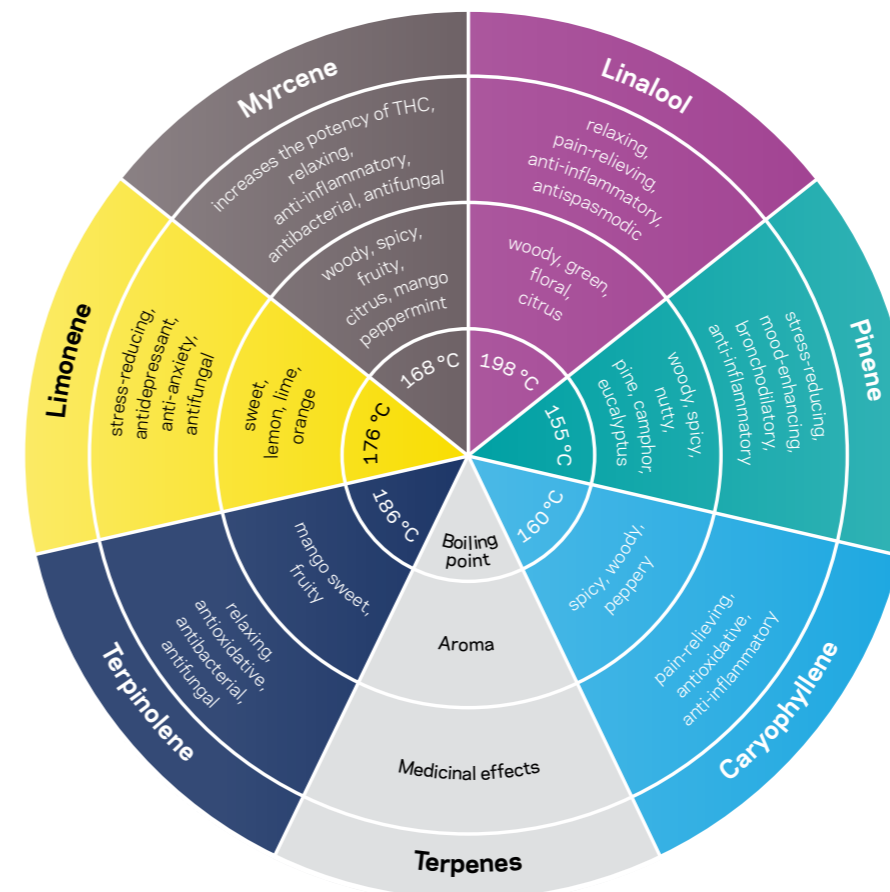
The cannabinoid system can be pharmacologically influenced and has an antagonistic effect on CB1 receptors. In contrast, externally supplied cannabinoids such as THC behave as agonists.⁵

Therapeutic Use

Pharmacological application – examples of potential effects

THC (Δ^9 -trans-tetrahydrocannabinol)	CBD (Cannabidiol)
<ul style="list-style-type: none"> ▪ Analgesic / antinociceptive⁶ ▪ Anti-inflammatory⁷ ▪ Neuroprotective⁸ ▪ Antioxidative⁹ ▪ Appetite-stimulant⁶ ▪ Muscle relaxant⁷ ▪ Antiphlogistic⁷ ▪ Antipruritic¹⁰ ▪ Antiemetic⁶ ▪ Sleep-inducing⁸ 	<ul style="list-style-type: none"> ▪ Antiphlogistic, antioxidative¹¹ ▪ Anti-inflammatory¹¹ ▪ Anxiolytic¹¹ ▪ Anticonvulsive, antispastic¹² ▪ Antiepileptic¹² ▪ Antimicrobial¹³ ▪ Skin therapeutic¹⁴ ▪ Addiction therapy for withdrawal treatment¹⁵

Overview of common terpenes



Terpene profiles

Terpenes are not psychoactive. However, they can still influence psychological processes by increasing the effects of THC. In this context, scientists speak of the entourage effect.

AURORA offers a large portfolio of different flower varieties with a range of terpene profiles that give each product an unmistakably unique aroma.

Effectiveness of terpenes

In addition to the main cannabinoids, the cannabis plant contains other therapeutically relevant ingredients such as terpenes and terpenoids. These volatile organic plant compounds are derived from the basic compound isoprene (C₅H₈) and occur mainly in plant resins and essential oils.

To date, about 200 different terpenes have been identified in the cannabis plant. The content and combinations of terpenes differ depending on the genetic origin of the plant. The proportions of these phytochemicals are largely responsible for the specific odour of different cannabis varieties and may have additional therapeutic benefits. Terpenes are found mainly in the flower hairs (trichomes) of the female cannabis plant.



The Entourage Effect

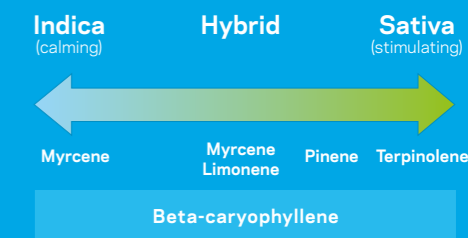
The special properties of terpenes also allow for suggested medically useful synergies with other plant substances. These synergies are described in relation to the family of cannabinoids under the collective term, the entourage effect.¹⁶

Terpenes can therefore influence the action of cannabinoids in different ways and vice versa. This is the result of different mechanisms: pharmacokinetic effects can improve the bioavailability and solubility of therapeutically useful components. In addition, the entourage effect can lead to a combined effect on various therapeutic target structures.

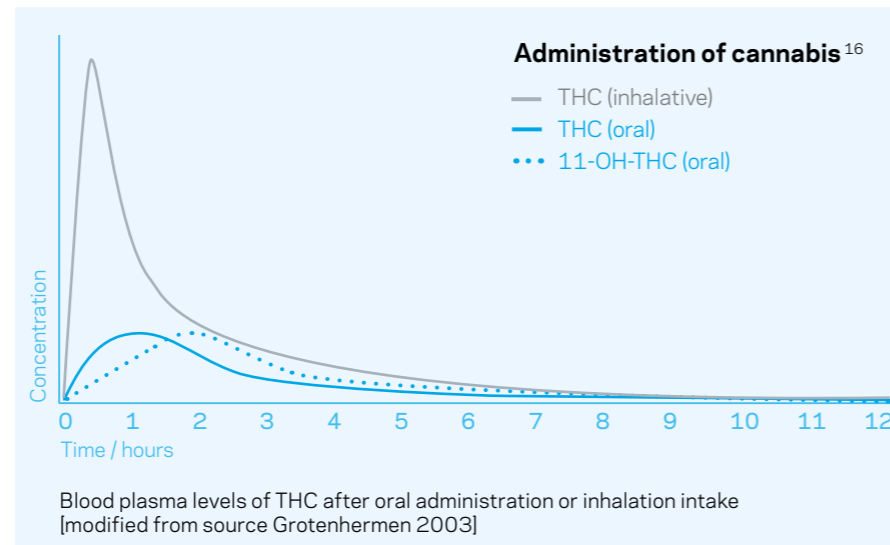
Many terpenes evaporate at temperatures similar to that of THC (157 °C) and are therefore also made available when cannabis is inhaled using a vaporiser.

Cannabis Sativa - The basics

The cannabis subspecies Sativa and Indica differ not only morphologically, but also in their terpene composition. This explains the different flavours and modes of action of the two subspecies: Indica varieties with the typical terpenes myrcene and caryophyllene have a calming and relaxing effect, whereas sativa varieties tend to contain terpinolene and pinene and are described as activating and stimulating.



Pharmacokinetics and Bioavailability



Cannabinoid pharmacokinetics: time dependence of THC and 11-hydroxy <-THC concentration in blood plasma

Administration	Onset of effect	Peak effect	Duration of effect
● Inhalative	< 5 min	10-30 min	2-3 hours
● Oral administration	30-120 min	2-4 hours	up to 12 hours or longer

Adapted from: <http://www.hc-sc.gc.ca/dhp-mps/marihuana/med/index-eng.php>

Dosing

Dosing dried cannabis flower

The general approach when initiating medical cannabis treatment is to start low, go slow, and stay low. Due to current limited clinical guidance for medical cannabis treatments, establishing an optimal dosing regimen requires a systematic trial-and-retrial approach.

Due to the varying effects of medicinal cannabis, treatment plans for similar indications are likely to be highly individualised. It is strongly recommended that doctors and patients have a constant, open dialogue about the impact of the cannabis product used.

Sativa, Indica, Hybrid: The Basics

The cannabis types (Sativa and Indica) differ not only in appearance but also in their composition and mode of action.

Indica is said to have a calming effect on both the body and mind while Sativa is claimed to be uplifting and cause more of a cerebral or 'head' high, with a combination of the two varieties being referred to as Hybrids.

Minimum effective dose

Individual dosing of cannabis flower enables the minimum effective dose (MED) to be established for each patient.

It is recommended to start with low dosages, monitor and discuss the effects, and slowly adjust the prescribed quantities (if needed) in order to achieve the desired symptom relief. This is commonly referred to as the "start low and go slow" approach. The optimal dose should relieve symptoms and improve functionality.

Start low, go slow, stay low!

Inhaled cannabis:

When cannabis is vaporised, THC enters the bloodstream and takes effect within minutes.

Cannabis taken orally:

As a preparation in oils or capsules, THC is absorbed and metabolised by the liver into the psychoactive substance 11-OH-THC or 11-COOH-THC.

Vaporisers

Cannabis flower can be administered by using devices known as vaporisers which heat the plant material to produce a vapor containing the active ingredients.

THC enters the bloodstream via the lungs and its effects are felt within minutes. Mighty+ and the Volcano vaporiser from Storz & Bickel are approved medical devices recommended for administering this form of medical cannabis.



Mighty+Medic Volcano Medic 2

Inhalation

Start: 1-2 inhalations

Effect: Felt after 10-15 minutes

Maintain the dose if the effect is sufficient. If the effect is insufficient, inhalation can be repeated 1-2 times.

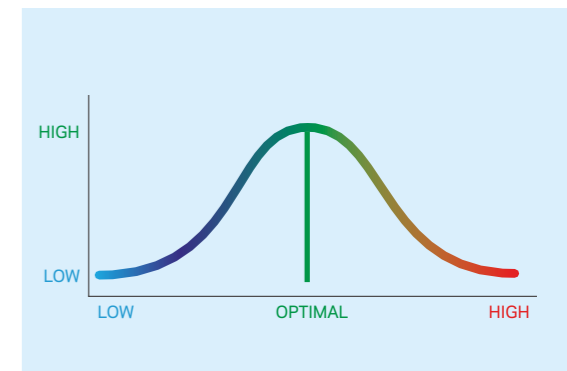
Repeat this step until the desired effect is achieved. After 6 inhalations without sufficient effect, the patient should consult a doctor to discuss further treatment.

The treatment plan (product, dosage, and form of administration) needs to be jointly refined and may change over the course of the treatment period.

Multiphasic dose-response relationship

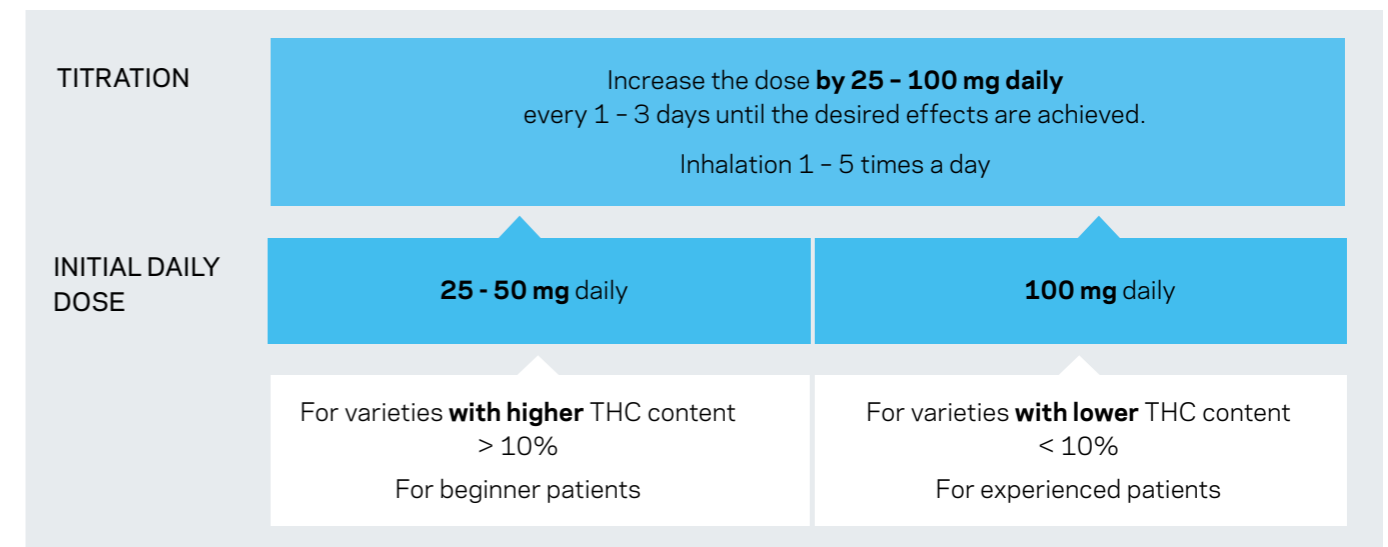
Cannabis has a unique dose-response relationship. For most medications, a higher dose is associated with a stronger therapeutic effect and a greater probability of adverse effects; this is known as a monophasic dose-response relationship.

Instead, while cannabis initially produces a greater effect when the dose is increased, after the optimal dose is reached any further increases may lead to weaker effects and even a reversal of the beneficial effects seen at lower doses. This is accompanied by an increase in unwanted side effects.



The medicinal benefits of cannabis may start to diminish as the dose is increased. (Dr. Sulak/Healer.com)

Titration of cannabis dried flower



THC Concentration in the Bloodstream²²

Studies have shown that approximately 50% of the cannabinoids contained in the hemp flower are found in the aerosol produced by the MIGHTY+ MEDIC. When this aerosol is inhaled, about 65% of the aerosol enters the bloodstream through the alveoli. The rest is exhaled. The medically effective cannabinoids THC and CBD behave in a similar manner.

Indicative values of THC in the blood after administration of the drug by vaporisation.

Vaporisation at a vaporisation temperature of 210°C. The following values are obtained for cannabis flower:

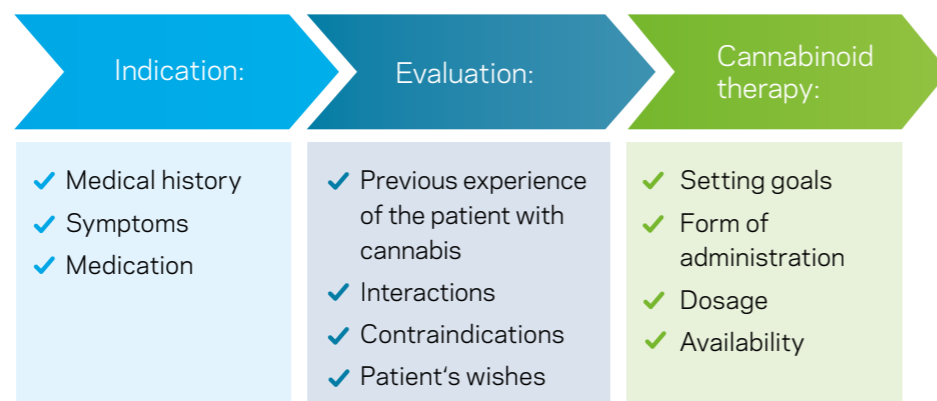
THC content in dried flower	THC content in 50 mg of cannabis flower	THC content in aerosol	Cannabinoid content in the bloodstream after inhalation	THC content in 100 mg of cannabis flower	THC content in aerosol	Cannabinoid content in the bloodstream after inhalation
10%	5 mg	2,5 mg	≈1.62 mg	10 mg	5 mg	≈3.25 mg
20%	10mg	5 mg	≈3.25 mg	20 mg	10 mg	≈6.50 mg
22%	11 mg	5,5 mg	≈3.57 mg	22 mg	11 mg	≈7.15 mg
24%	12 mg	6 mg	≈3,90 mg	24mg	12mg	≈7,80 mg
26%	13 mg	6,5mg	≈4,22 mg	26mg	13mg	≈8,44 mg
28%	14mg	7mg	≈4,55 mg	28mg	14mg	≈9,10 mg

In order to reach these values, the patient must inhale until no more vapour can be seen during exhalation. The contents of the filling chamber are then exhausted.



Prescribing information

How do I find the right variety for the individual patient?



Due to the different effects of medicinal cannabis, the treatment plan for similar indications can be highly individualised.

It is strongly recommended that doctors and patients maintain an ongoing and open dialogue about the effects of the medicinal cannabis product being used.

AURORA cannabis flower product overview

The AURORA dried cannabis flower spectrum. In 2024, Aurora GmbH introduced an innovative new colour-coding scheme to differentiate its cannabis products by strength. The new product packaging features green, blue and purple in ascending order of THC strength.

Ultra High THC		PEDANIOS 31/1 COS-CA Cultivar: Cosmic Cream (Indica)	<ul style="list-style-type: none"> ▪ analgesic / antinociceptive⁶ ▪ antiemetic^{6,9} ▪ myorelaxant⁷ ▪ sleep-inducing / sedative⁸
Super High THC		PEDANIOS 29/1 SRD-CA Cultivar: Sourdough (Indica)	<ul style="list-style-type: none"> ▪ analgesic / antinociceptive⁶ ▪ anti-anxiety⁸ ▪ antiemetic^{6,9} ▪ myorelaxant⁷ ▪ sleep-inducing / sedative⁸
High THC		PEDANIOS 22/1 Cultivar: Ghost Train Haze (Sativa)	<ul style="list-style-type: none"> ▪ analgesic ▪ antinociceptive⁶ ▪ antiemetic^{6,9} ▪ appetite-stimulant⁶ ▪ anti-anxiety⁸ ▪ neuroprotective⁸
Balanced		PEDANIOS 10/10 EQI-CA Cultivar: Equiposa (Hybrid)	<ul style="list-style-type: none"> ▪ analgesic²³ ▪ antinociceptive⁶ ▪ myorelaxant⁷ ▪ anticonvulsive, antispastic¹² ▪ antiepileptic¹²

Contradictions²⁴

According to Health Canada's recommendation, the risk/benefit of medicinal cannabis use needs to be carefully and individually considered for those:

- Under the age of 18
- With a history of hypersensitivity to any cannabinoid or smoke (if the cannabis is smoked)
- With severe cardio-pulmonary disease with occasional hypotension (low blood pressure), possible hypertension (high blood pressure), syncope (loss of consciousness), and tachycardia (rapid heart rate)
- With respiratory diseases such as asthma or chronic obstructive pulmonary disease (COPD)
- Patients with severe liver or renal disease, including chronic hepatitis C
- With a personal history of psychiatric disorders or a family history of schizophrenia
- With a history of substance abuse
- Of childbearing age and not on a reliable contraceptive, planning to become pregnant, pregnant, or breastfeeding
- In addition, medical cannabis should be used with caution in individuals with mood disorders or those taking sedatives or other psychoactive drugs

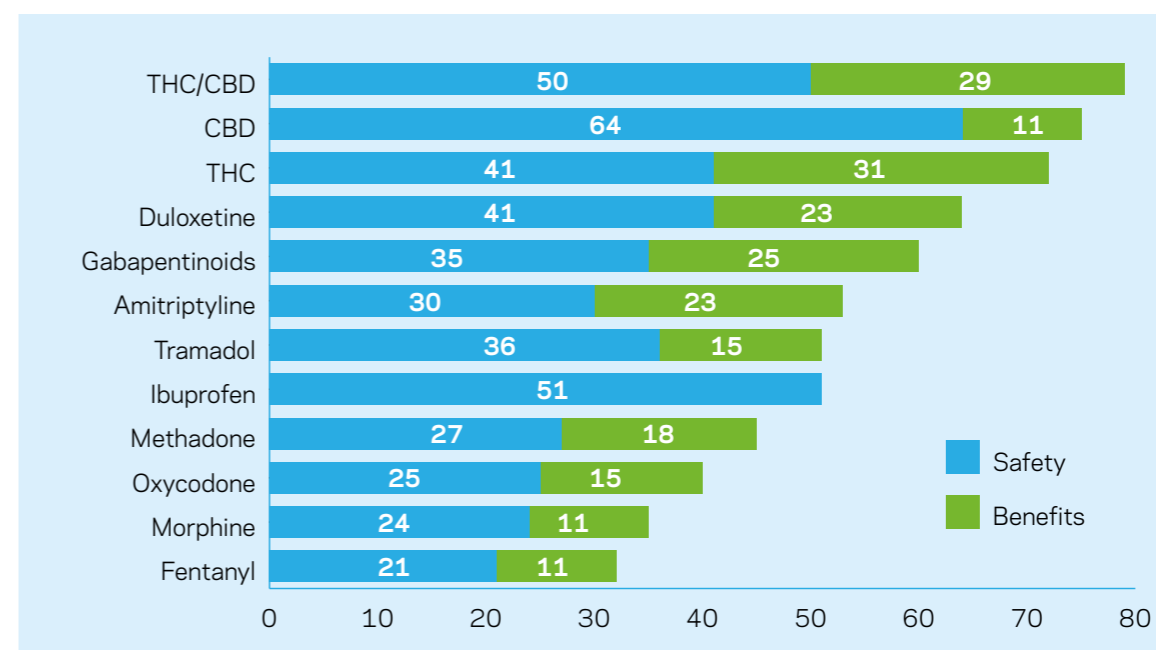
Side effects

Common, acute side effects include:

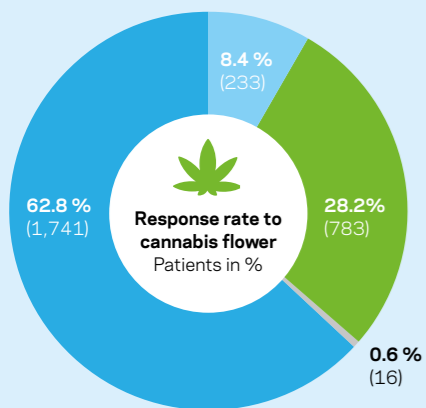
- dizziness
- dry mouth
- euphoria
- nausea and vomiting
- fatigue and somnolence

Due to habituation effects resulting from regular use, medical cannabis is generally considered to be well-tolerated.⁹

Benefit-Safety Balance³²



Response rate to cannabis flower



A 2022 survey by the German Federal Institute for Drugs and Medical Devices (BfArM) on the use of cannabis medicinal products evaluated 2,773 datasets.²⁸

- Significantly improved
- Moderately improved
- Unchanged
- Significantly worsened

Interactions

Both delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are metabolised by the cytochrome P450 enzyme system, mainly by CYP2C and CYP3A4.²⁵

- In vitro studies have shown an inhibitory effect of THC and CBD on the isoenzymes CYP1A1, CYP1A2, and CYP1B1. In addition, CBD is a potent inhibitor of CYP2C19 and CYP3A4.²⁵ Concomitant use of other drugs that induce, inhibit or are substrates for the CYP3A4 isoenzyme may require dose adjustment to avoid a lack of efficacy or increased side effects.
- In addition to interactions at the metabolic stage, medical cannabis may also have pharmacodynamic interactions involving synergistic effects with other drugs. This may include benzodiazepines, opioids, or phenobarbital.²⁶
- Enhancement of effect by concomitant use of potent CYP3A4 inhibitors:²⁷
 - clarithromycin
 - ketoconazole
 - indinavir
 - lopinavir
 - ritonavir

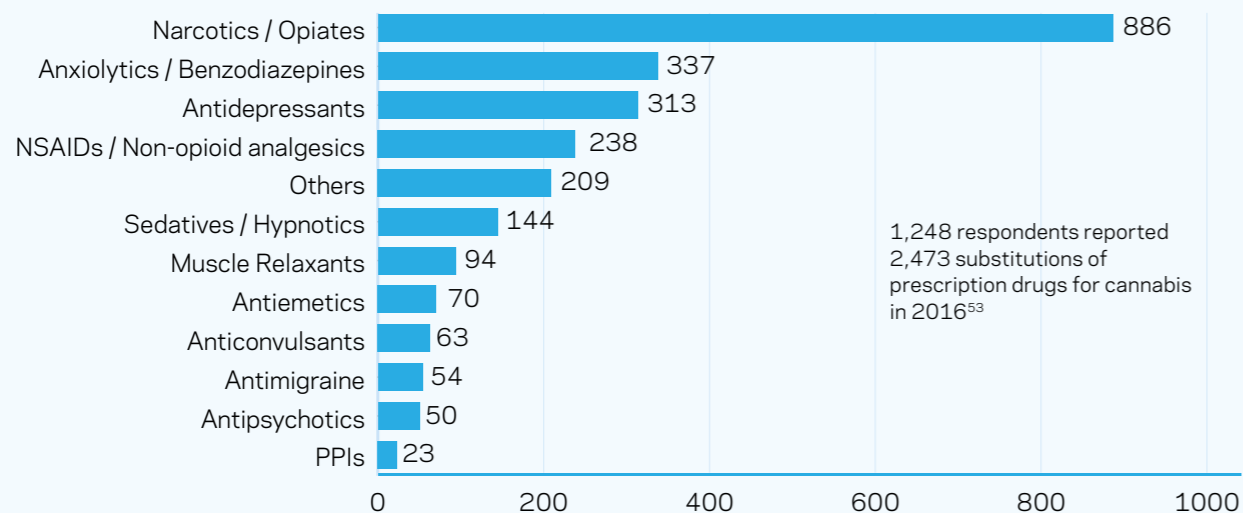
91% of patients benefit from cannabis flower therapy with a mild side effect profile.

Reduction of opioids and opioid-induced side effects

There is also considerable evidence that cannabis is effective as an adjunct therapy for pain management.

Cannabinoids and opioids are believed to act synergistically to relieve pain.^{29,30} As a consequence, medical cannabis products can reduce opioid doses among chronic pain patients receiving high doses of opioids.

Cannabis vs. prescription drugs ³¹



Conclusion:

There is a great need for medical cannabis products to treat a wide range of complaints.

Indications for cannabis medicinal products include chronic pain, tumour- and non-tumour-related pain, and spastic pain in multiple sclerosis.²³ Patients with chronic pain cannot usually be treated using a monotherapy approach and can benefit from an add-on therapy with cannabinoids.

Benefits of Aurora Cannabis Flower

- Complementary therapy for patients with ailments such as chronic pain
- Contains all the essential substances from the cannabis plant
- Favourable side effect profile compared with opioids
- Produced in Canada under strict EU GMP requirements
- Our available formulations make it possible to tailor the treatment to the needs of individual patients
- Fast onset of inhaled cannabis flower compared to oral application

AURORA Medicinal Cannabis

In order to fulfil individual therapy requirements and different areas of application, we offer a wide range of products.

Security of supply thanks to EU GMP-certified production facilities in Canada.

Cannabis flower

By leading the way in plant breeding and genetic research, Aurora's science and innovation team is building a sustainable pipeline of new plants with innovative traits that are set to transform the way the world uses cannabis.



Cultivation

Medicinal cannabis refers to the dried female flowers of the Cannabis plant and the pharmaceutical-grade dosage forms produced from them. Medicinal cannabis is produced from cuttings. This means that all plants of a variety have the same genetics and have identical properties.



Specification

Aurora follows the highest standards such as GACP (Good Agricultural and Collection Practice) and GMP (Good Manufacturing Practice) in cultivation, production, product release and dispatch. These guarantee the consistently high quality of our products. Genetic stability and maximum controlled growth conditions guarantee constant active ingredient concentrations with a maximum deviation rate of 10%. This ensures a high level of patient safety.



Sterilisation

Contamination with potentially pathogenic germs should be ruled out, especially when used via inhalation, e.g. by immunocompromised patients. For this reason, all Aurora cannabis flowers are sterilised using electron beam irradiation. This method reduces the bacterial count in a particularly gentle way.



About us

Aurora UK Medicine Ltd. is part of Aurora Europe. Headquartered in Berlin, Aurora is a subsidiary of Aurora Cannabis Inc. (Alberta, Canada), a global leader in the cannabis industry serving both the medical and consumer markets and dedicated to helping people improve their lives. The company supplies high-quality medical cannabis products to patients throughout Europe.

Improving access in the UK

Following the change in legislation in November 2018, Aurora became one of the first companies to supply medical cannabis in the UK, even though access remains a challenge for patients. Aurora is working to help the UK assume a leading role in patient advocacy and create a medical cannabis system that works. To achieve this, the company is building its reputation as a trusted partner for physicians, patients, and regulatory authorities by continuing to supply high-quality medicinal cannabis products and investing in clinical research, physician education, and continued patient advocacy.

www.auroramedicine.com

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