SW4Partners

LawrenceStephens*

ARTEMIS GROWTH PARTNERS

Extracting Opportunities

Contents

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Key findings

'Extracting Opportunities' explores the dynamic and rapidly evolving extract-based medical cannabis market in Europe. This report dives into the transition from traditional cannabis forms to advanced products such as tinctures, capsules, creams, and vape cartridges, underscoring their pivotal role in broadening market appeal and delivering targeted medical benefits.

This report is a must-read for anyone seeking opportunities in the medical cannabis sector. It includes a comprehensive understanding of the industry landscape and discusses the prospect of extract-based medical cannabis in Europe, combining detailed analysis with engaging content to illuminate both the complexities and opportunities within this burgeoning sector.

Key Discoveries:

- **Diversification of the Market:** Extract-based products are reshaping the consumer base, attracting new demographics.
- **Tailored Medical Solutions:** These products are increasingly being developed to address specific medical needs, bolstering their therapeutic impact.
- Precision in Dosing: Consistent potency is revolutionising prescribing practices, enabling more precise treatment.
- **Focus on Quality:** Top-grade ingredients are necessary for the development of pharmaceutical-quality products.
- **Growth and Opportunities:** The European extract market is growing rapidly and continues to present ample opportunity for expansion.

Introduction

The landscape of medical cannabis in Europe and global markets is evolving, with extract-based products playing a pivotal role in the transformation towards a more robust pharmaceutical cannabinoid market. Medical professionals and patients are increasingly gravitating towards extract-based cannabis-based products for medicinal use ("CBPMs") over flower, with formulated products setting new benchmarks in quality and therapeutic potential.

'Extracting Opportunities' explores how the extracts market is one of the fastest growing segments of the European medical cannabis market, with the potential for further growth as regulations come into place and cannabis medicines become further destigmatised.

Extracted Products ("Extracts" or "EPs") such as capsules, creams, vape cartridges and sublingual solutions, have broadened appeal beyond traditional flower, expanding the addressable market to a significantly larger group of patients.

Extracts facilitate targeted treatment of specific symptoms and conditions, offering a level of customisation that can be difficult to achieve with traditional pharmaceutical medicine. A range of formulated products are being developed to address specific symptoms and indications with targeted properties, like rapid onset or sustained duration. This can be particularly beneficial for patients with complex drug resistant or difficult-to-treat conditions.

Extractss also offer a level of control and predictability that is indispensable in a clinical setting, with their consistent potency eliminating the variabilities that traditionally occur with cannabis flower. Consistent potency ensures uniform dosing, simplifies clinician prescribing and monitoring, and enables robust data collection to facilitate research trials which we believe will further expand the market.

One of the critical drivers to Extracts is Precise Dosage Control. Extracted cannabis products like oils, tinctures, and edibles can be precisely measured, making it easier to control the dosage. This is especially important for medical use, where specific dosages may be recommended for different conditions.

- **Accurate Dosing:** Extracted products allow for precise measurement of dosage, which is crucial for medical treatments. This precision helps doctors prescribe specific amounts of active ingredients (like THC and CBD), tailored to each patient's needs.
- **Ease of Use and Compliance:** Non-inhalable forms can be easier for some patients to use, especially those who are elderly, very young, or otherwise unable to smoke. This can lead to better compliance with the treatment regimen.

Flexible Administration Methods: With a variety of product forms (oils, tinctures, topicals, etc.), doctors can choose the most suitable method of administration for each patient, considering factors like the patient's age, condition, lifestyle, and personal preferences.

This research explores how extract-based medical cannabis products have the potential to revolutionise the field, diving into the importance of high-quality extracts and the burgeoning market for standardised, high-quality cannabis inputs among drug developers and manufacturers.

1. The Market

Access Routes for Extract-based Medical Cannabis Products

Extracts represent an increasing proportion of Europe's medical cannabis markets, available through both licensed and unlicensed channels depending on the country and its legal framework. There are several key routes through which Extracts are accessed in Europe:

'Licensed Pharmaceutical' Model: Limited scale of European adoption

Medical products that have gone through a conventional pharmaceutical approval process and are prepared for specific indications. At present, there are just two medically proven natural cannabis plant-derived products, both from GW Pharma: Sativex and Epidiolex. In addition to these, two cannabinoid products that use synthetically-sourced inputs have been developed, containing the active ingredients Nabilone and Dronabinol.

Given that these are medically proven products, typically, approval is not subject to specific political or narcotics control issues. These products have been approved for a limited set of indications:

These products represent a small percentage of the European market, unlike unlicensed cannabis extracts (in the form of finished products or Active Pharmaceutical Ingredients (APIs)) for pharmacy compounding. Off-label use of licensed medicines bears potential risks for physicians and is only feasible when the cannabinoid profile fits the patients' needs, whereas unlicensed CBMPs can enable treatment of a broader range of conditions.

Full Spectrum Oils

Whilst pharmaceutical products have their place in the value chain, full spectrum oils can offer a wider therapeutic offering than approved drugs like Epidiolex, Sativex, Marinol, and Cesamet due to the entourage effect. Studies including Gallily et al (2015)1 highlight the increased effectiveness of full-spectrum cannabis extracts compared to isolated CBD, particularly in the context of a more favourable dose-response relationship.

These products can also be made available at a more affordable cost. For example, iIn several countries, including the UK and France, availability of these productspharmaceutical CBMPs is also restricted due to value-for-money or efficacy concerns from health regulators.

Product	Indication	Active Ingredients	Format
Epidiolex®	Rare epilepsy syndromes	Cannabidiol, CBD isolate	Oral solution
Sativex®	Muscle spasticity in multiple sclerosis (MS)	Nabiximols, broad-spectrum extract	Oral spray
Marinol® / Syndros®	Chemotherapy-induced nausea and vomiting, neuropathic pain	Dronabinol, synthetic THC isolate	Oral capsules or solution
Cesamet ®/ Canemes®	Chemotherapy-induced nausea and vomiting	Nabilone, synthetic isolate	Tablet

Whilst pharmaceutical products have their place in the value chain, full spectrum oils offer a wider therapeutic offering than approved drugs like Epidiolex, Sativex, Marinol, and Cesamet at a more affordable cost. In several countries, including the UK and France, availability of these products is also restricted due to value-for-money or efficacy concerns from health regulators.

In the absence of clinically validated products for each target condition, countries have taken one of two routes; the 'purchase authorisation' model as seen in the US, Canada and Israel, or the 'unlicensed medicines' model as seen in most of Europe.

'Purchase Authorisation' Model: No European adoption

Rather than issue a prescription for a specific product, healthcare practitioners register or 'authorise' patients with qualifying medical conditions to obtain medical cannabis products. Patients may then purchase products directly from licensed producers, as in Canada, or, in the case of US states, from medical cannabis dispensaries.

Conventional pharmaceutical standards are not required for the cultivation and manufacturing of medical cannabis products. Many North American early adopters of medical cannabis have subsequently instigated regulated, adult-use markets.

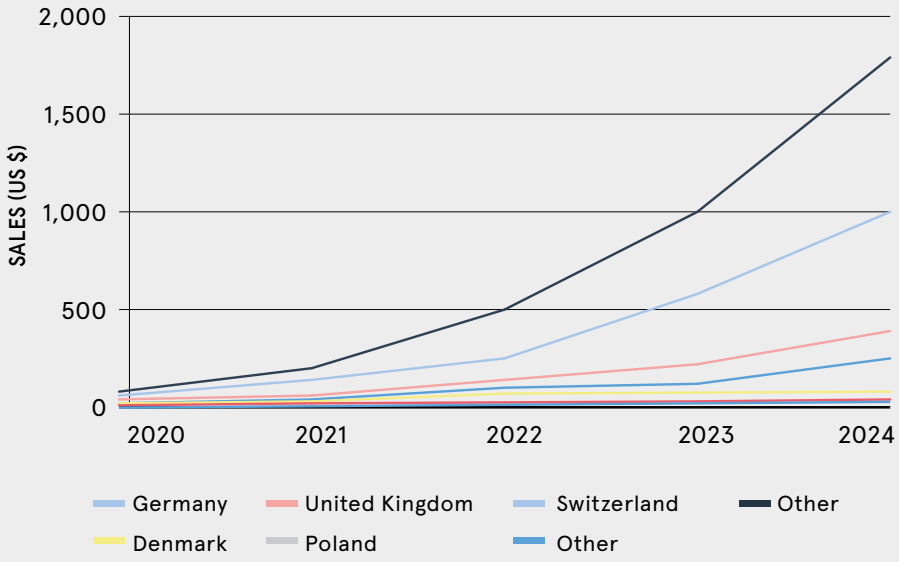
'Unlicensed Medicines' Model: Most prominent route of access in Europe

In the UK, most EU Member States, Australia and New Zealand, CBPMs are accessed through a process more closely aligned to the traditional medicines framework.

In such models, CBPMs are typically treated as an unlicensed medicine with cultivation, processing, packaging and distribution required to conform to established pharmaceutical standards. Prescriptions are written for a specified product, cannabinoid content and dose, and are dispensed by pharmacists.

As a result of the stringent quality requirements at each step of production, CBPMs in such markets can command a higher cost-per-gram or unit of active ingredient than North American jurisdictions. Doctors and pharmacists' close involvement in the prescription, monitoring and supply of CBPMs also allows for the greater collection of patient and observational data and reinforces institutional support for the generation of further clinical evidence around efficacy and safety.

Extract-Based Finished Products
(Without Marketing Authorisation)



Source: Prohibition Partners, The Cannabis Extraction Report (2022)

Access Routes under the 'Unlicensed Medicines' Model

European countries have taken different approaches to bringing CBPMs under an 'Unlicensed Medicines' model, with variations in the range of product formats on offer and who is authorised to supply the market. Some countries like the UK take a more liberal approach, permitting imports of hundreds of products from many global licenced suppliers, while others like Italy have established supply tenders for fixed quantities of product, supplemented by domestic cultivation, overseen by the Italian military.

Several key models (non-discrete) are emerging in Europe:

UK and Australia

Finished Dose Products

CBPMs typically do not require further manufacturing steps by the pharmacy, other than checking and affixing the prescription.

CBPMs are supplied in a ready-to-dispense format with fixed dosing. In limited instances, products may be manufactured or tweaked by a local pharmacy for special clinical cases.

Portugal and Denmark

Market Authorisations / Individual Product Approvals

Some countries require a separate product authorisation process for CBPMs that have not received full market authorisation.

This includes Portugal, where CBPMs must receive either a full marketing authorisation (AIM), or an Authorization for Placement on the Market (ACM) to be sold in Portugal.

The ACM registration procedure has been simplified for cannabis plant preparations and extracts, and has reduced registration requirements including no need to demonstrate clinical efficacy. Securing an ACM does not make a CBPM a 'licenced' medicine in the typically understood sense (ie. Sativex or Epidyolex).

For example, Tilray Portugal received an ACM in February 2021 for a dried flower product. The ACM is valid for five years, subject to renewal under the terms of the following article. After the first renewal, ACM is considered to be valid indefinitely, unless the Portuguese Health Authority Infarmed has reason to determine that the renewal is only valid for five years.

Extracted products (ie. oils or capsules) are likely to be better suited to achieving ACMs instead of flower, as product dosage must be precise and consistent to achieve authorisation.

France and Ireland

Early Access Patient Schemes

Some countries have opted to implement small-scale, more cautious pilot programs to gather evidence before expanding access to CBPMs to the wider population base.

For example, France's pilot program was launched in March 2022 to allow medical cannabis on a trial basis for up to 3 years. It aims to gather data on the effectiveness and safety of CBPMs before deciding whether to make them available to the wider population.

The pilot allows a limited number of patients to access CBPMs on prescription. To be eligible, patients must have certain conditions like epilepsy, cancer-related pain, multiple sclerosis, or palliative care needs that are resistant to conventional treatments.

Germany, Italy and Poland

Pharmacy Compounding / Magistral Preparations

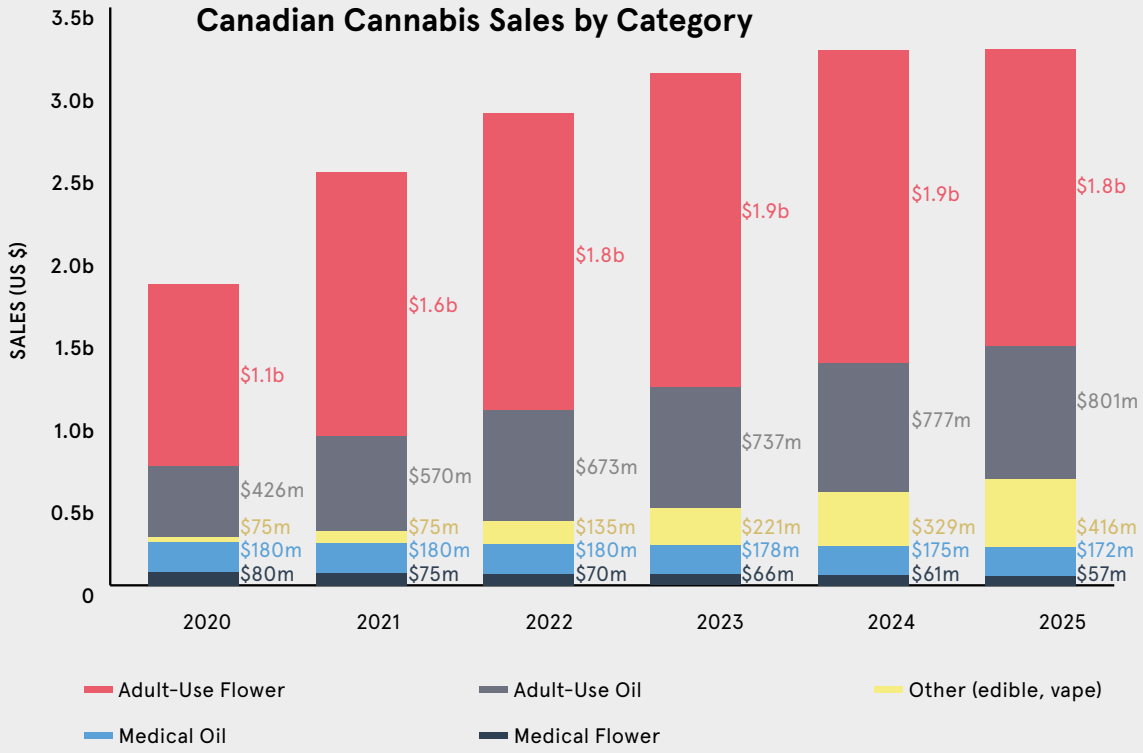
CBPMs are classified and dispensed through pharmacy compounding (also referred to as magistral preparations) rather than as 'finished medicinal products'. The product is considered as a bulk/intermediate until it is dispensed. This requires pharmacists to undertake the final compounding/ manufacturing step before dispensing to patients.

Using this method, pharmacies directly compound flower, or extracted APIs, into CBPMs based on the doctors' prescription. The compounding process can range from simply rebottling or measuring a supplied product, all the way to manufacturing tailored formulations.

Countries like Germany have established monographs for permitted CBPM formats and manufacturing processes, with the German Pharmacopoeia commonly used as a reference in Europe.

2. Doctor-Patient Dynamics

While the initial focus of the medical cannabis industry was on flower products, there has been a clear shift towards Extracts in both Europe and North America. Formats such as soft gel capsules, transdermal creams, and vape cartridges are designed to extend the benefits of flower to a wider patient and clinician audience.



Source: Prohibition Partners, The Cannabis Extraction Report (2022)

Non-flower CBPMs are becoming increasingly popular, offering consistent, quality alternatives that resemble conventional medicines. These products cater to patients who either cannot or choose not to smoke cannabis. Their rise is driven by their precision in dosing, standardised formulations, and user-friendly administration, leading to enhanced patient adherence and improved therapeutic outcomes.

Historical challenges, such as inconsistent dosing, lack of standardisation, and varied delivery methods associated with traditional cannabis use, are addressed by these extract-based CBPMs. They provide a range of delivery methods and strengths, allowing for tailored treatment plans that align with individual therapeutic needs.

This evolution towards accuracy and reliability in the medicinal cannabis field promises better clinical outcomes and an improved quality of life for patients. These modern formulations not only eliminate the intake of unnecessary contaminants like biomass and waxes but also ensure efficient delivery of active components with high bioavailability or to specific body areas.

Doctor Dynamics

In European markets, doctors are the primary point of access for CBPMs. They determine if a patient should receive CBPMs, the type of product to be prescribed, and the dosage. This decision often hinges on the concentration of cannabinoids, from high-THC to high-CBD products. The frequency, volume, and duration of the prescription are also determined during these consultations, with follow-up appointments scheduled for potential adjustments.

Some European countries have set restrictions on which doctors are able to prescribe CBPMs. In countries like the UK, general practitioners are unable to prescribe CBPMs, leaving only specialist doctors in fields such as neurology, gastroenterology, and psychiatry the legal authority to do the same. Their expertise regarding the specific conditions and the range of treatment options in their field means that they may be sceptical of 'new' alternatives, particularly if they are in a totally unfamiliar format like flower for inhalation.

The legal and medical framework for cannabis is in flux. For doctors juggling a myriad of medical concerns, staying updated on the latest research, legislation, and clinical best practices related to cannabis can be daunting. The majority of CBPMs in Europe are currently unlicensed, meaning they lack specific marketing authorisations for specified conditions.

Products that are simple for doctors to learn about and prescribe, with fixed dosage formats that enable monitoring, will be key to expanding the CBPMs market to a wider demographic.

Advantages of Extract-Based Products for Doctors	
Standardised Dosing	One of the primary advantages of Extracts is the ability to offer a consistent and measurable dosage. This ensures that patients receive the exact amount prescribed, eliminating the guesswork and potential risks associated with variable dosages.
Consistent Potency	Through the process of extraction and refinement, uniform strength is guaranteed, ensuring that each dose is as effective as the last.
Ease of Administration	The streamlined nature of these products simplifies the prescription process. Doctors can more easily monitor patient intake, ensuring safety and efficacy.
Guaranteed THC Absence	For patients who may have adverse reactions to even trace amounts of THC, Extracts can be tailored to ensure complete absence, providing peace of mind to both doctors and patients.
Robust Trials	The standardisation inherent in Extracts allows for more rigorous and reliable clinical trials. This not only advances scientific understanding but also paves the way for broader market access and regulatory acceptance.

Patient Dynamics

Patients receiving CBPMs can be broadly divided into two groups based on their prior use, awareness, and confidence in using cannabis, with certain formats being more suitable for each group.

Group A	Group B
Cannabis-naive patients with limited experience of medical and/or recreational consumption	Patients experienced in self-medicating with cannabis

For both groups, Extracts provide a more accessible, traditional alternative to flower. As more CBPMs formats become available, the market dynamic is set to shift to greater adoption of these form factors.

Group A:
Cannabis-naive patients with limited experience of medical and/or recreational consumption

- This group is likely to have persistent clinical needs that have been unmet by other treatments, and those who are keen to reduce their reliance on pain and other medications.
- Patients are interested in learning more about cannabis and how it can be used to treat their condition, gaining insight from doctors directly as well as patient community groups.
- They are generally more reliant on doctor recommendations, clinical evidence, and wrap-around services to guide their treatment decisions.

Patients that are more accustomed to traditional pharmaceutical products naturally lean towards CBMP formats like capsules, tablets, and oils. These formats closely resemble well-established pharmaceutical offerings, including tablets, capsules, oral solutions, creams, and oral sprays—commonly associated with over-the-counter essentials such as pain relievers, throat sprays, and topical creams.

Familiarities with existing pharmaceutical products

Tablets	Capsules	Oral solution	Creams	Oral sprays
				

The familiarity of these formats seamlessly aligns with conventional medical practices, making them appealing to prescribing physicians and a natural choice for patients. In contrast, the direct consumption of flower may seem unconventional and unfamiliar in a medical context.

Group B: Patients experienced in self-medicating with cannabis

- This group tends to have a deeper understanding of the compounds present in the plant and how to use them to treat their symptoms.
- Additionally, they are generally more aware of visual and flavour profiles, growing conditions, and genetics of the plant.
- Patients in this group are often confident researching and evaluating the products available to them and conveying a preference to their prescriber. They may be willing to 'shop around' and switch prescribers to gain access to desired products.

Many individuals with prior experience using flower or vape products from the legacy cannabis market often find themselves comfortable using these formats (CBPMs) for their therapeutic needs. However, several factors can sway them towards more conventional pharmaceutical formats.

The transition of legacy patients from flower to extract-based CBPMs is often motivated by concerns related to stigma, especially when using CBPMs in professional or public settings or around family and children. Extract-based products offer a discreet and socially acceptable alternative, with formats like capsules easily fitting into a patient's daily routine.

These patients may also be motivated by the health advantages of this transition, as ingesting or vaping extracts is less harmful than combusting flower due to the absence of tar and other combustion-related byproducts. Extract-based CBPMs offer a consistent dosage, in contrast to flower, which can vary in potency, ensuring patients receive a dependable and uniform amount of active compounds with each use.

3. Product Breakdown

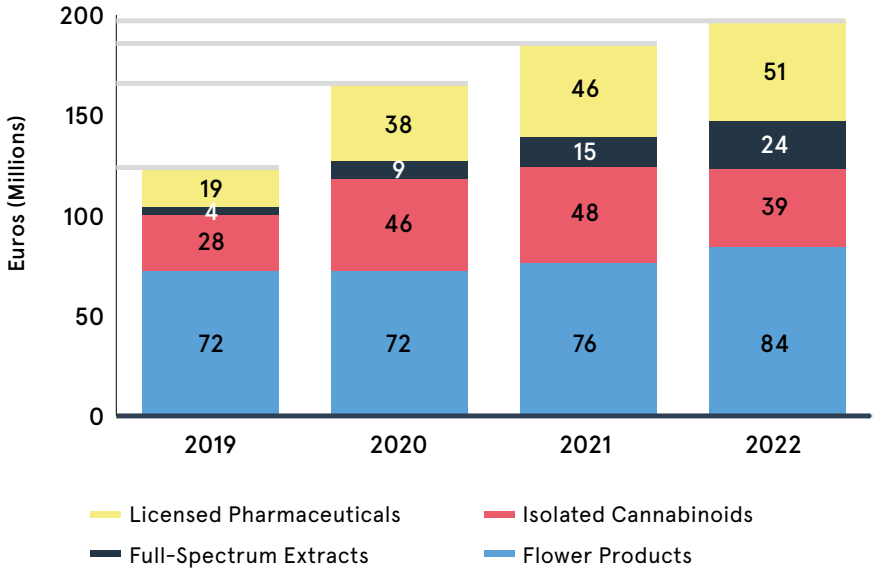
The conventional practices of smoking or inhaling cannabis flower are typically viewed with scepticism by regulatory bodies and medical experts. They deem it a potentially harmful method of administration.

A discernible shift can be observed as nations appear to be gravitating towards extract-based prescriptions, distancing themselves from flower-centric treatments. For example, insurance companies in Germany appear to be increasingly inclined to grant reimbursements for medical cannabis products in extract-based formats at a higher rate compared to flower-based alternatives. Insurance companies face a more challenging argument in contending that drops or extracts are not pharmaceutical, while the acceptance of flower-based CBPMs retains certain stigmas within the medical context.

"In Germany, insurance companies are reluctant to subsidise recreational-style cannabis flower use. They consider pharmaceuticals, such as drops and pills, as the standard, distinct from smoking. As the cannabis flower market expanded, it became evident that many were potentially receiving free joints for minor ailments. Extracts offer a treatment-oriented approach for major conditions like cancer, epilepsy, and multiple sclerosis, due to their distinct effects and longer absorption time. In the context of socialised medicine, extracts align closely with pharmaceutical forms, making it challenging for insurance companies to argue against their inclusion within coverage."

Michael Sassano,
Somai Pharmaceuticals

Public Health Insurance Coverage of Medicinal Cannabis in Germany, € millions



Source: German National Association of Statutory Health Insurance Funds (GKV-Spitzenverband)

Notably, recent developments, as detailed in an arbitration ruling from June 17, 2022, have significantly impacted reimbursement policies. The ruling led to a substantial reduction in the reimbursable base price for German-grown cannabis flowers, from EUR 9.52 per gram to just EUR 4.30 per gram. This reduction has the potential to make flower-based products less attractive and less profitable for pharmacies, thereby further encouraging the adoption of extract-based medical cannabis products.

"Simply providing patients with raw flower and having them self-titrate doses could be dangerous, like sending someone home with a handful of unnamed painkillers. Physicians accustomed to prescribing in milligrams per millilitre often initially lean towards liquid extracts that match this familiar precision dosing.

The clarity of standardised, measurable doses that extracts provide is paramount for physician comfort with prescribing cannabis as a medical therapy. Compared to flower products with more variability, extracts in formats like oils, gels and capsules enable exact, consistent dosing that physicians understand and trust when treating patients."

Pete Patterson,
Valcon Medical

Product Formats

Across the multiple access pathways - licensed pharmaceuticals, finished-dose unlicensed products, and unlicensed magistral preparations - various extract-based CBPMs are accessible. Each format presents distinct benefits, whether in dose duration, bioavailability, or ease of administration. This wide array of options broadens the potential market for CBPMs, catering to a diverse set of use cases, indications, and symptoms.

Format	Overview	Advantages	Use Cases
Oral Drops	Liquid solutions containing cannabis extracts. Typically administered under the tongue using a dropper.	Discreet and precise method of dosing. Sublingual administration allows for faster absorption into the bloodstream compared to ingestion.	Used for a variety of medical conditions, including pain management, anxiety, and sleep disorders.
Vaporisable Extracts	Cannabis extracts heated by a device to produce a vapour that is inhaled, typically in the form of cartridges.	Provides immediate onset of effects. Vaporising offers a healthier alternative to smoking as it doesn't produce harmful tar and carcinogens.	Can be used in situations where quick results are needed, such as during migraine onset, acute pain or panic attacks.
Oral Sprays	Sprays that deliver cannabis extracts directly into the mouth.	Like oral drops, they offer a discreet method of dosing and can be easily carried around.	Suitable for those who might find drops cumbersome or for those who prefer a spray mechanism.
Soft Gel Caps	Soft gelatine capsules filled with cannabis oil.	Provide a consistent dose and are easy to swallow. Effects are longer-lasting compared to inhalation methods. Discreet consumption method.	Ideal for long-term symptom management, and chronic conditions where sustained relief is required, such as chronic pain or insomnia.
Transdermal Creams	Creams, ointments or patches infused with cannabis extracts that are absorbed through the skin.	Provide localised relief without systemic effects. Can target specific areas of pain or inflammation without affecting the entire body.	Used for conditions like arthritis, muscle pain, or skin conditions.

The CBPMs prescribed should align precisely with the patient's diagnosis and needs, rather than taking a one-size-fits-all approach. Different patients require tailored solutions.

"In Germany's medical cannabis market, there is a separation between self-payers who pay out-of-pocket and those reimbursed by insurance. Among self-payers, the demand has primarily been for lower cost dried flower products and specific strains, hinting at recreational motivations.

However, seriously ill patients who obtain insurance reimbursement tend to use more expensive, precisely dosed extracts for their medical value. This divergence has shaped the market dynamics in Germany, where pharmacies field frequent requests for trending strains while insurance often reimburses standardised cannabinoid therapies."

Peter Emil Sigetty,
Valcon Medical

Pharmacy Compounded Products (Magistral Preparations)

CBPMs compounded in pharmacies, also referred to as magistral preparations, utilise inputs such as flower and extracted APIs. These APIs can be in the form of individual cannabinoids or full-spectrum extracts. Germany has a national formulary (DAC / NRF) that outlines the types of CBPMs that pharmacists can formulate. The primary formats are bottled oils or oil allocated into capsules. For instance, a prescribed format of 25ml/mg applies to dronabinol drops, with a preference for CO_2 extraction and the use of MCT oil in extracts.

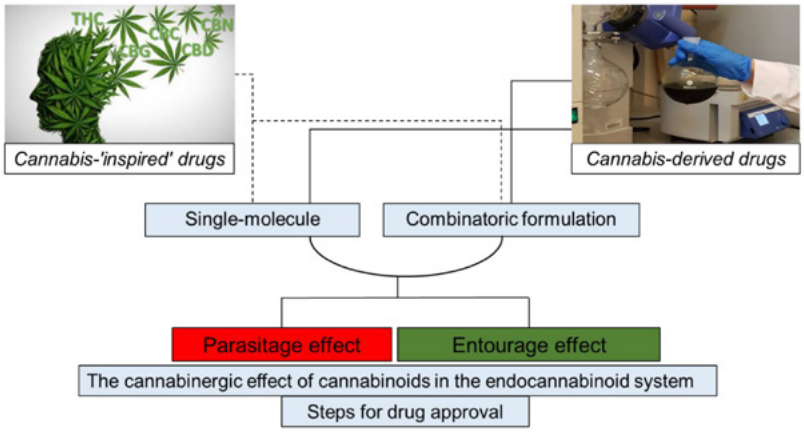
Inputs for these preparations include dried flower, which the pharmacist formulates based on the doctor's prescription specifications, alongside full-spectrum extracts, which are extracted oils with a range of cannabinoid content. In addition to these, several companies now provide dispensing kits for German pharmacies. These kits simplify the process, allowing pharmacists to supply extract-based CBPM prescriptions with fewer compounding steps.

Beyond dried flower, isolated cannabinoids, such as dronabinol, can be used in prescription preparations. This segment is seeing increased market share. In Europe, dronabinol (whether synthetic or plant-derived) serves as both a generic version of Marinol® and as an API for pharmacy compounding, especially in countries like Germany, Austria, and Switzerland.

Synthetic and Plant-Derived APIs

APIs can originate from two primary sources: plants or synthetic processes. Synthetic cannabinoids eliminate the need for heavy metal and pesticide testing, but still require checks for microbiological factors and cannabinoid content. Lab-created synthetic isolates can sometimes be more costly and harder to source than plant extracts. This cost difference often stems from the intricate production processes associated with synthetic forms. Despite their prevalence in medical and pharmaceutical sectors, synthetic products often face scepticism from the general public. For example, natural extracts are typically the preferred choice for consumer wellness products.

Synthetic APIs	Chemically synthesised in laboratories
Natural APIs	Derived from natural sources like plants
Biotechnological APIs	Produced using biotechnology processes



4. Market Supply

Extraction Techniques

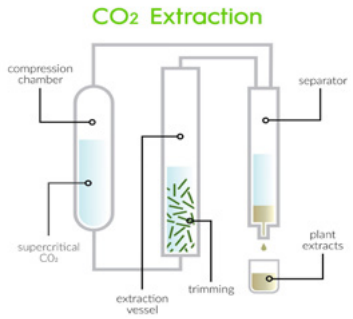
The cannabis industry has seen a surge in innovation and development in the field of extraction techniques, given their central role in product quality. These methods are a crucial step to produce high-quality cannabis products, allowing for the separation of valuable components of the plant, such as cannabinoids and terpenes, from the plant matter.

CO2 Extraction

CO2 extraction is often favoured over solvent-based extraction techniques due to its purity and safety. The two methods differ in several aspects, such as efficiency, operational costs, process intricacy, terpene preservation, facility features, environmental impact, and even the stance of regulatory bodies.

CO2 Extraction

Also known as supercritical fluid extraction, this method uses carbon dioxide under high pressure and fluctuating temperatures to isolate the desired chemical compounds from the cannabis plant. This technique is known for its efficiency and purity, producing high-quality cannabis oil without any residual solvents. It also preserves essential terpenes and cannabinoids. The process requires expensive, sophisticated equipment and skilled operators, which can be a barrier for some producers.



CO2 extraction can produce pharmaceutical grade isolates and distillates.

Pros	Cons
Safety: CO2 extraction is considered one of the safest methods as it doesn't involve the use of potentially harmful solvents. **Purity:** This method often results in a pure and clean extract, free from chlorophyll and other unwanted compounds. **Efficiency:** CO2 extraction can be fine-tuned to extract specific compounds, making it highly efficient.	**Cost:** The initial setup cost for CO2 extraction equipment can be high. **Complexity:** Requires skilled operators and precise conditions for optimal results.

Solvent-Based Extraction Methods

Solvent-based methods involve the use of solvents to dissolve the plant's trichomes and extract cannabinoids and terpenes. This method is popular due to its cost-effectiveness and ability to produce high yields. However, it comes with the risk of leaving residual solvents in the final product if not properly purged, which can be harmful if consumed.

Hydrocarbon Extraction

Butane and propane, known as hydrocarbon solvents, are efficient at capturing the complete essence of a cannabis variety. They operate at low boiling points, allowing for the extraction of all cannabinoids and terpenes without the use of extreme pressures or temperatures. However, scaling these systems can be costly due to the safety precautions required.

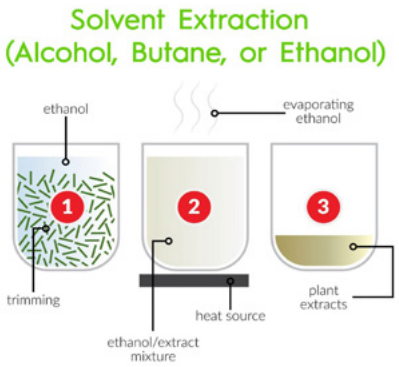
Hydrocarbon extraction can produce full spectrum extracts.

Pros	Cons
Potency: Often results in a highly potent extract.	**Safety:** Uses flammable solvents like butane or propane, posing potential safety risks.
Flavour Preservation: Retains the terpenes and flavonoids, preserving the plant's natural flavours.	**Residual Solvents:** Risk of residual solvents remaining in the final product if not properly purged.

Ethanol Extraction

Safer to operate than hydrocarbon solvents, ethanol requires no pressure to extract compounds from plant matter. It binds extremely well with cannabinoids and terpenes but also with unwanted compounds such as fats, waxes, and chlorophylls, which can affect the product's quality. This issue can be mitigated by chilling the ethanol to -40 Fahrenheit, leaving behind most of these unnecessary compounds.

Ethanol extraction produces simple cannabinoid isolates and distillates.



Pros	Cons
Versatility: Suitable for both small-scale and industrial applications.	**Purity Concerns:** May extract unwanted compounds like chlorophyll, affecting the final product's taste and colour. This may necessitate further processing.
Speed: Faster extraction times compared to other methods.	**Safety:** Ethanol is flammable, necessitating careful handling and storage.

Process and Outputs

A range of bulk and intermediary formats are manufactured as inputs for CBPMs. Potency increases as products become more refined and isolated, bringing the extract closer to a pharmaceutical than the composition of the whole plant.

Format	Overview	Potency	
Cannabis Flower	Contains over 400 biologically active substances	15-20%	Closer to the whole plant
Crude Extract	Unrefined extract containing plant materials like chlorophyll and fatty acids	40%	
Refined Oil	Extract that has been processed to remove waxes and plant material and decarboxylated	70%	
Distillate	Highly concentrated extract that has been distilled into a fraction	90%	Closer to a pharmaceutical
Isolated Cannabinoid	Single-molecule extract. CBD and THCA crystallise in their pure form, while THC and CBDA resemble oily substances.	99%	

Production Innovations

A key focus for the medical cannabis industry is research and development of new and existing products, technologies for cultivation, extraction and manufacturing, delivery mechanisms, genetic composition of cannabis and combinations of cannabinoids, and ultimately research and trials regarding the efficacy and safety of CBPMs.

Europe is currently at the forefront of introducing novel innovations to the market. Simultaneously, operators are assimilating advancements from major markets such as North America and Israel to develop more potent and effective CBPMs for patients.

Nanoemulsions	Nanoemulsions employ a technology that converts cannabis oils into water-soluble formulations, which amplifies their absorption and bioavailability upon intake. By reducing cannabis compounds to nano-sized particles, typically within the range of 20-200 nanometers, they can circumvent the body's innate digestive mechanisms more effectively. This not only facilitates a swifter onset of effects but also optimises the therapeutic potential of cannabinoids. The reduced and consistent particle sizes also ensure that cannabinoids are uniformly dispersed, resulting in a more consistent patient experience.
Live Resin	Live resin is a specialised form of extract obtained by flash-freezing fresh cannabis flowers followed by hydrocarbon-based extraction. This method retains a significantly higher terpene content, endowing the resin with a richer flavour and aroma. Additionally, the potency of the product is typically elevated due to the preservation of cannabinoids during the extraction process.
Solventless Extraction Methods	Enzyme-assisted extraction (EAE) has emerged as an innovative method for producing high-quality, solventless cannabis oils. Developed by Italian company Herbolea Biotech, EAE uses enzymes to efficiently extract desired compounds from fresh cannabis biomass mixed with a carrier oil. The enzymes facilitate release of cannabinoids and terpenes, generating a potent full-spectrum extract. A key advantage of EAE is the ability to derive exceptionally high terpene content from fresh plant material, achieving concentrations up to 22 times higher than CO2 extracts from dried biomass.

5. Operator Landscape

The operator landscape for extract-based CBPMs is fledgling and varied. A range of operating models are being pursued. Some companies are striving for vertical integration and a suite of branded products, while others have opted to focus on contract production, the supply of bulk and intermediate derivatives, and white label services.

This section spotlights leading European operators, highlighting recent innovations and novel market solutions.

Operator	Country	Full spectrum extraction and API	Branded finished products	Magistral kits
Somai Pharmaceuticals	Portugal			
Valcon Medical	Denmark			
Avextra	Germany			
Brains Bioceutical	Canada			
Grow	UK			
Vayamed	Germany			
Linnea	Switzerland			
Panaxia	Israel			
CBDepot	Slovenia			

Somai Pharmaceuticals

Portugal

Somai Portugal Pharmaceuticals Ltd is a European biotech firm that specialises in the development and production of cannabinoid-infused pharmaceutical products. The company's goal is to introduce a diverse range of plant-derived medical cannabis formulations to both the European and international markets.

Situated in Lisbon, Portugal, Somai's facility spans 3,800 sqm, with the capability to expand up to 10,000 sqm. This strategic location not only offers a robust manufacturing base but also ensures efficient access to European and global markets. Somai has successfully completed Phase 1 of its facility construction and was awarded EU-GMP certification from the Portuguese Health Authority INFRAMED in September 2023. Phase 2, currently ongoing, focuses on expanding the production area and enhancing the cleanroom facilities. Phase 3 is set to incorporate a hydrocarbon extraction unit, positioning Somai to deliver an even more diverse range of products, including edibles and concentrates.

The facility's modular design is geared towards scalability, allowing it to adapt to increasing market demands. Somai expects to generate first revenues in 2023 of c.EUR 3 million with substantial growth in 2024 to c.EUR 17 million.

Somai is developing a comprehensive portfolio of CBPMs that includes oral drops, sprays, soft gel caps, transdermal patches, and sublingual strips. To enhance the efficacy of these products, the company is working on introducing two carrier mixes in Europe, aiming for improved therapeutic onset and better absorption rates. Somai has also developed vaporisable extracts that contain a combination of THC distillate and terpenes.

At its core, Somai is committed to addressing the distinct needs of patients. The company is gearing up to launch an initial set of 65 products, each tailored with specific THC:CBD ratios. This lineup will cater to a spectrum of patient preferences, from high THC to balanced and high CBD formulations. Alongside this, Somai is actively participating in absorption trials, focusing on their advanced carriers and specialised formulations.

Somai is bullish about the growing potential of extracts, recognising a need in the market for more tailored cannabis-based medicines. They anticipate a shift in medical professionals' preferences towards extracts, especially as more refined products become available. Somai intends to be at the forefront with a vision of continuous innovation, offering a broad range of CBPMs under a unified brand.

"Alike to traditional pharmaceuticals, countries like Germany are moving towards implementing 'Over-the-Counter' ('OTC') markets, where products will not require prescription from a doctor and medical cannabis is no longer deemed a narcotic. The addressable market will be rapidly expanded, with a much broader set of products gaining traction outside of the strict prescription framework. High quality, effective products will be demanded from the outset, and Somai will be able to immediately leverage its future-proofed product range.

We are the brand that has every single product distributors are looking for. They don't have to worry about whether we're going to be out of stock, it is going to always be there, and we will have every product ready for the foreseeable future."

Michael Sassano,
Somai Pharmaceuticals

Grow / IPS

UK

Grow is one of the UK's largest suppliers of CBPMs and was the first company to import medical cannabis into the UK after it was legalised in 2018. Grow Pharma was established by Grow Biotech and IPS Pharma, combining cannabis sector expertise with 18 years' experience manufacturing and importing unlicensed medicines.

Dean Gainsley, Grow Group's Non-Executive Director, shared his perspectives on the level of uptake for extract-based CBPMs in the UK medical market.

How have patient preferences influenced the market offering?

"At the infancy of the UK's medical cannabis sector, the industry lacked the capabilities of more mature markets such as the US. As a result we saw flower and oils becoming the dominant pathways. Additionally, early adopters of medical cannabis in the UK had often used flower when self-medicating illicitly and indicated preferences towards the format.

However, for much of the wider population, the concept of grinding and inhaling flower for medical purposes remains too foreign and tied to stigma, with many expressing discomforts around medicating with children in proximity. While oils provide a more discrete alternative, they come with a strong earthy taste and tend to coat the teeth and inside of the mouth. Capsules have performed better than oils in the more mature North American markets but can be expensive.

I think pastilles (gummies) are likely to become a popular format, with the small amount of sugar aiding digestion and flavourings disguising the taste of the raw inputs."

What has held back prescription of extract-based CBPMs in the UK to date?

"I think the UK is now on the cusp of embracing extracts aside from basic oils. To date, this has been held back by several factors. Supply chains have struggled due to the lack of GMP capacity, both in terms of sourcing inputs and manufacturing products. Formats like gummies and tablets can be particularly challenging to manufacture under GMP, where every input and manufacturing process is subject to audit.

Another factor has been cost. In the UK, vape cartridges are currently being manufactured in clean rooms at a very small scale, being filled individually by hand. This has meant that the cost of a cartridge is noticeably more expensive than purchasing the equivalent potency in flower, and incurs a higher price point than cartridges available via the illicit market."

Valcon Medical

Denmark

Valcon Medical was incorporated in 2018 as a Denmark-based medical cannabis company focused on extraction. Headquartered in Copenhagen, Valcon is a leading European GMP contract manufacturing organisation, offering a complete outsourcing solution covering every phase from formulation and development to the delivery of finished product. Valcon distributes medical cannabis products to European markets including Germany, Poland, Denmark and the UK.

Valcon's team and staff bring a wealth of knowledge from the pharmaceutical industry and the company is positioned as such; EU-GMP certified, state of the art production facility, and focused on developing robust product data sets tailored to the requirements of each market.

As a result of variations in legal frameworks, Valcon Medical has needed to employ different strategies to enter each market:

Denmark:

In Denmark's medical cannabis system, once a CBPMs is validated, manufacturers file for approval from the Danish Medicines Agency to market the product. Approved medicines are then available for doctors to prescribe and visible on a public list of authorised CBPMs. The manufacturer supplies products to central consignment storage facilities. When prescribed, two major distribution companies deliver the CBPMs from storage to pharmacies. Pricing is set by the manufacturer, with distributors and pharmacies taking fixed percentages.

Germany:

For the German market, Valcon delivers CBPMs directly to pharmacies in various forms, either in their original packaging or as a raw product. The exact process can vary depending on the pharmacy chain or individual pharmacy; the pharmacy might repackage or relabel the product. Some provinces, like Bavaria, are stricter than others in terms of compliance and the distinctions between finished and intermediate products.

This decentralised approach, where pharmacies perform small-scale preparations, has presented limitations in efficiency and standardisation. Over time, as demand has risen, the market has shifted towards licensed producers supplying more pharmacy-ready products and preparation kits. These enable larger scale, more consistent production methods with standardised dosing and formulations for patients.

Other markets:

In the UK, Valcon adopts a white label model like that implemented in Germany, where their product is marketed under the brands of other companies. For the Polish market, Valcon supplies raw extract material, which local partners can formulate and standardise into CBPMs. This flexibility to tailor their offerings - whether white label finished products or bulk raw materials - has enabled Valcon to expand across Europe despite the diversity of CBPM regulations in different countries.

"Finished formats are permitted in Germany, but you need to go through a full clinical trial. The magistral pathway opened a bit of a loophole to be able to allow physicians to prescribe it and for cannabis producers to be able to put products into the market. Doctors were looking for a route to bring medical cannabis to their patients, and found this would be possible if the product was manufactured by a pharmacy.

The system is a continuously evolving mechanism. In the early stages of the medical cannabis program, producers would provide a concentrated cannabis extract to pharmacies, who would then dilute the extract in MCT oil and bottle it for patients. Pharmacies are limited in how much they could produce at one time, typically around 100 units per batch."

Pete Patterson,
Valcon Medical

Panaxia

Israel, Malta

Panaxia is one of the leading medical cannabis companies in Israel, with operations across key European markets. Founded in 2010 and headquartered in Lod, Panaxia operates two EU-GMP extraction facilities in Israel and Malta, two extraction facilities in Poland, and one extraction facility in the US. The company was the first company to receive a production license from the Israeli Ministry of Health (IMC-GMP) and the first company in Israel to receive a European certification (EU-GMP). Panaxia specialises in developing and producing pharmaceutical-grade CBPMs, including oils, extracts for inhalation, tablets, and suppositories containing varying ratios of cannabinoids like THC and CBD and unique formulations based on minor cannabinoids, terpenes, and flavonoids for specific indications. They supply about 10% of the German cannabis extract market, over 50% of the French cannabis market, and over 90% of the Polish extract market.

After receiving EU-GMP certification in 2017, Panaxia has collaborated internationally, partnering with companies like Neuraxpharm, Rafa Laboratories, and Axionovo for global distribution. In 2019, Panaxia established a subsidiary called Panaxia Labs Europe in Malta to manage its European operations and business development. They obtained an EU-GMP license from the Malta Medicines Authority in 2020 to produce and export CBPMs to EU markets. Panaxia set up an extraction and production facility in Malta to manufacture pharmaceutical-grade medical cannabis oils and extracts for the European market. Panaxia Labs Europe has partnered with major distributors like Neuraxpharm in Germany to supply CBPMs across Europe. Panaxia Europe currently markets cannabis extracts in Germany, France, Poland, CH, CZ, Cyprus, and Malta, and was the first company to introduce cannabis extract for inhalation in Europe (Germany, Poland, and Malta).

They have also collaborated on clinical trials and R&D partnerships with European universities and companies. The EU division focuses on expanding Panaxia's reach in Europe beyond Israel, given the larger addressable market and evolving regulations.

Brains Bioceutical

Canada

Brains Bioceutical is an evidence-based and science-led pioneer of cannabinoid health and wellness solutions. Brains Bio produces natural cannabinoid Active Pharmaceutical Ingredients (APIs) to unlock therapeutic innovation in health care and mitigate the risk of quality-related failure in clinical trials.

Operating out of its EU-GMP and MHRA-licensed facility—the largest of its kind in Europe—Brains Bio has consistently produced over 450 batches of CBD API. Their APIs are in more than 30 pre-clinical and clinical trials worldwide, encompassing both FDA, MHRA, and TGA approved studies. Brains Bio has secured long-term supply contracts with top-tier global pharmaceutical entities and research and academic institutions. Brains Bio's cannabinoid API R&D initiative includes D9 THC (solid and oil), D8 THC solid, CBN and CBG. In collaboration with DSM-Firmenich, Brains Bio continues to chart new frontiers. Together, they are developing innovative formulations to enhance loading, bioavailability, solubility, and specificity, including pioneering finished dosage forms tailored for medical and pharmaceutical applications.

6. Regulatory Environment

International Regulations and Trends

We have seen in the earlier parts of this paper how the extracts market is one of the fastest growing segments of the European medical cannabis market, with the potential for further growth as regulations come into place and CBPMs become further destigmatised. We should not forget that cannabis for medicinal purposes has been widely legalised in many jurisdictions. Legislation and patient access of CBPMs are two separate elements which differ from country to country.

UNITED KINGDOM

In the UK the laws changed in 2018 to allow the prescription of CBPMs, the main legislation being the Misuse of Drugs Act 1971 (MDA 1971) and Misuse of Drugs Regulations 2001 (MDR 2001). The Medicines and Healthcare products Regulatory Agency's (MHRA) are responsible for unlicensed medicines (Manufacturers Specials licence) - and the requirements for prescribing, importation, manufacture, distribution and dispensing of CBPMs.

One of the main issues in the UK is the barrier to patients accessing CBPMs, as CBPMs cannot be prescribed by general practitioners (GPs) and not easily funded by the NHS. The MDR 2001 was amended in 2018 rescheduling cannabis in the UK including a provision that restricted the prescribing of CBPMs to those doctors who were specialists and listed on the General Medical Council (GMC)'s Specialist Register.

It is our view that the UK would become a major player in Europe for prescriptions of CBPMs, if GPs were better educated on the benefits of prescribing them, and more importantly, if there were an amendment to legislation to allow GPs to prescribe with a model that allowed these prescriptions to be fully funded or partly funded in the UK.

GERMANY

In Germany the following must be observed:

i. German Narcotics Act (*Betäubungsmittelgesetz*, BtMG).

ii. Section 31 para.6 of the German Social Security Code Vol 5 (*Sozialgesetzbuch Fünftes Buch*, SGB V), specifically concerning patients receiving reimbursement from public health insurers under certain circumstances.

iii. German Medicinal Products Act (*Arzneimittelgesetz*, AMG) covers the importation of CBPMs (covering manufacturing and trading of medicinal cannabis).

The German market is currently seen as one of the prominent medical cannabis jurisdictions in Europe because of the level of prescriptions, attributed to patients receiving reimbursement from the public health insurer and the UK could learn from the reimbursement model by making it more accessible on the NHS.

It is our understanding that the public health insurer is being pushed to reduce the price of reimbursement from EUR 9.52 to EUR 4.30 on cannabis flower (CBPMs). This seems to have been calculated solely on the basis of the German Drug Price Regulation (Arzneimittelpreisverordnung or AMPreisV). The effect of lowering the reimbursable base price for of cannabis flowers makes such flowers less profitable and potentially less attractive for pharmacies in Germany.

This could be seen as a clear indicator leading to producers and distributors focusing on extracted CBPMs which would in theory be more attractive for the German pharmacist.

PORTUGAL

There are variety of laws and legislation concerning cannabis in Portugal. The regulatory body for enforcing the laws and regulations on cannabis and cannabinoids for medical purposes in Portugal is INFARMED – the National Authority of Medicines and Health Products, I.P. (Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.).

Portugal is quickly becoming an integral player within Europe in the production of cannabis raw material (flower) and Extracts. According to data from Infarmed, it is understood that circa. 61 licenses have been granted as at the end of 2022. The make up of these licences were: 20 cultivation, 8 R&D and extraction/processing, 23 for import/export, and 10 for marketing related companies. Again the UK could learn from the Portuguese regulator on making such licences more accessible to allow more home-grown production.

Portugal has been seen as the California state of Europe when it comes to cultivation and extraction.

Although the Portuguese medical cannabis market is both extremely well regulated and established there are still some obstacles to overcome regarding patient access of CBPMs.

Another main issue for the Portugues market is the price of CBPMs. We must not forget however in the grand scheme of things the population of Portugal is relatively small when it comes to patients.

FRANCE

In March 2021 France commenced a pilot programme on therapeutic cannabis, it was set up with the goal of enrolling circa. 3,000 patients over a two-year period to assess the feasibility of the supply, prescription and delivery of CBPMs to patients for whom no other therapeutic alternative is available.

As at 23rd October 2023 the French Government tabled an amendment to the Social Security Financing Bill (PLFSS) concerning medical cannabis, bringing it into France's general medical framework.

The key points of the amendment are:

- CBPMs will receive 'temporary authorisation' for five years, with the potential of renewal by the Agence Nationale de Securite du Medicament et des Produits de Sante (ANSM) for a further five years.
- Products will be authorised on a case-by-case basis.
- Flowers and all other inhaled forms of cannabis are excluded.
- The current experiment comes to an end in April 2024 and there will be a maximum of nine months to allow the transition to take place.
- A budget of €10m (5 x the current budget) has been allocated for the transitional period.
- Access to CBPMs will continue to be restricted to a last-resort treatment, and prescribed in hospitals.
- The criteria for prescription of CBPMs will be set subsequently by decree following an upcoming proposal from the ANSM.

The writers are of the view that once the legal framework is developed to allow prescription of CBPMs, it should be expected that the French market will flourish in the same way as that of its neighbour Germany.

DENMARK

The Danish medicinal cannabis pilot programme started 1 January 2018 which allowed doctors to prescribe types of cannabis products for medicinal use. The Danish Medicines Agency has assessed that CBPMs should be considered only for a few different conditions for which there is supporting evidence of the positive effect and only for ailments such as: painful spasms caused by multiple sclerosis or spinal cord damage, nausea after chemotherapy, and neuropathic pain.

Originally the pilot programme was planned to expire at end of December 2021. However, the Danish Ministry of Health published its evaluation of the pilot programme at the end of November 2020 which led to a debate amongst health professionals and experts concluding that the pilot programme provided a proper and safe framework for the use of cannabis for medicinal purposes. The evaluation further showed that patients associations and the cannabis industry wished for the programme to become permanent or to continue for an additional number of years before turning permanent.

Notwithstanding this, at the start of 2021, former Minister of Health, Magnus Heunicke, initiated political discussions regarding the future of the pilot programme, and in December 2021 (the original expiry date) it was sanctioned that there would be a renewal of the pilot programme.

The pilot programme is due to come to an end on 31 December 2025. However, the Minister of Health is required to re-evaluate the position by the end of 2024.

NETHERLANDS

In the Netherlands the Dutch Opium Act sets out drugs with a low risk of harm (`soft drugs') from drugs with a high risk of harm (`hard drugs').

Cannabis is listed under the soft drugs category (Category II), which effectively means its tolerated under certain circumstances for recreational use.

CBPMs have been legal since 2003. Although the Dutch framework is well established all activities concerning CBPMs are strictly regulated.

CBPMs are subject to the Dutch Medicines Act, a marketing authorisation is required to bring a product to market. Patients have

access to CBPMs through their pharmacies, provided they have a prescription.

AUSTRALIA

The Australian Government legalised access to medicinal cannabis in 2016. The supply is regulated by the Therapeutic Goods Administration (TGA).

As in the EU and the UK CBPMs are unregistered. To prescribe these products, a doctor must have approval from the TGA. This can be via the Special Access Scheme-B or Authorised Prescriber Scheme. Within Australia the laws are different in each state / territory which may affect whether patients can access CBPMs.

Medical cannabis approvals through the Authorised Prescriber (AP) scheme in Australia have seen substantial growth, according to data from TGA. It is understood that in the first half of last year, AP approvals reached approximately 304,000, marking a remarkable increase of more than 120% compared to the same period last year, when there were 137,000 AP approvals. The growth has been attributed to the rising number of authorised prescribers, which surged from 175 in 2020 to 636 in 2021 and further to 1,454 in 2022. This provides a strong case study for the UK, demonstrating the significant impact that increasing the number of eligible prescribers has on patient uptake.

The Special Access Scheme (SAS-B) route for patient approvals for CBPMs has also witnessed notable developments. In 2021, patient approvals via the SAS-B pathway soared to nearly 122,000. There was however a slight decline in 2022, with 117,000 approvals, as patients shifted towards the AP pathway. In the first half of 2023, SAS-B approvals have reached approximately 87,000. Interestingly, the most prevalent "dosage form" for SAS-B approvals in 2023 has been medical cannabis in the form of oral liquid, with 44,345 approved applications[1].

1 Source: Therapeutic Goods Administration (TGA).

National Regulations

The regulatory landscape for medical cannabis in Europe is fragmented, with no unified set of guidelines governing its access and use. Countries have their own framework determining the availability of extract-based products, their sourcing, and the legislative basis for access, be it through permanent laws or time-bound pilot studies.

A snapshot of the regulatory environment in some of Europe's major markets is outlined below.

Country	Medical 2022	Medical 2025	Domestic Cultivation	Finished Dose Extracted Products	Magistral Preparations (Compounding Route)
Net Importers					
Germany	€248m	€973m	Y	N	Y
Italy	€31.3m	€85.5m	Y	N	Y
UK	€25m	€533m	Soon	Y	Limited
Poland	€11.8m	€122m	N	N	Y
Switzerland	€3.4m	€53m	Y	Y	Y
France	-	€160m	N	Y	N
Net Exporters					
Netherlands	€5.9m	€7.7m	Y	N	Y
Denmark	€8.5m	€105m	Y	Y	Y
Portugal	€0.8m	€2.1m	Y	Y	N
Netherlands	€5.9m	€7.7m	Y	Y	Y
Spain	-	€155m	Y	Licensed medicines only	N

Market Sizing Source: Prohibition Partners, 2022 (6th Ed)

7. **Conclusions:** Looking Ahead

The European market for extract-based CBPMs exhibits strong promise for exponential growth in the coming years as availability increases and regulations continue to develop. Advanced formulations are likely to serve as a catalyst to fully integrate cannabis into mainstream pharmaceutical practice.

Doctor Willingness to Prescribe
A 2022 PLOS One study found 67% of surveyed clinicians across Europe expressed willingness to prescribe CBPMs, indicating shifting attitudes. As stigma declines and medical education around cannabis intensifies, doctors will likely feel more comfortable integrating cannabinoids into treatment regimens.

> **The UK industry at present is dominated by prescription of flower and oil. Indeed, over 99% of prescriptions are for those two formats with virtually no other method of administration available. This is shame and other forms of extracted product are urgently needed. Both doctors and patients would value the availability of other formats. Tablets or soft gel capsules, for example, are a more familiar way of taking medicine than oil, let alone a flower for vaping. Standard medical inhalers, for further example, are a more familiar and acceptable form of administration for airway use. Some patients will benefit from patches or suppositories for their condition. These different modes are far more acceptable to the general public and indeed to their doctors – many of whom simply do not want to consider prescription flower or oil. That is too "recreational" for many and we really need to allow cannabis to be considered as a normal medicine, prescribed in familiar ways. It is time that the extraction market rose to the challenge.**

Professor Mike Barnes,
Honorary Professor of Neurological Rehabilitation Maturing Regulatory Environment

More defined legal frameworks governing CBPM access are emerging across European countries. As of 2023, CBPMs are legal in 30 out of 44 countries in Europe, with patient numbers increasing across these markets. Prohibition Partners projects the European cannabis market will reach €37 billion by 2027, with Germany standing as the largest medical market at €7.7 billion. With continued dialogue between policymakers and industry leaders, we can expect even more streamlined regulations that foster growth and patient accessibility.

> **The European cannabis extracts market is on a trajectory of significant growth, driven by expanding legalization, a rising demand for medicinal cannabis, and the introduction of new product formats. Quality control, a reliable supply chain, and patient education will be critical factors shaping the market's future. Regulatory developments, research, and continued market consolidation are also key factors to monitor as this dynamic industry continues to evolve.**

Pete Patterson,
Valcon Medical Research
and Clinical Validation

Robust clinical research and trials focused on medical applications of cannabis extracts are accumulating. A 2021 review in the European Journal of Internal Medicine found over 100 controlled trials demonstrating efficacy of cannabinoids for indications like chronic pain, spasticity, nausea, sleep disorders, and Tourette's. Ongoing trials aim to further validate cannabinoids as first or second line treatments. Strategic R&D partnerships between producers, academia, and pharmaceutical companies remain integral to CBPM development. The next decade may witness breakthrough findings, solidifying cannabis' role in addressing previously untreatable conditions.

> **Our company's commitment to clinical research, improved potency, efficacy and enhanced safety profiles continues to remain the main force behind our drive for success. By having the largest EU-GMP cannabinoid R&D and commercial facilities, we have positioned Brains Bio to be the number one supplier of safe, natural cannabinoid API's. Our team continues to set the highest and most stringent production standards in the industry.**

Ricky Brar,
Brains Bioceutical Broadening Product Diversity

The diversity of CBPMs caters to specific patient populations and preferences. Conventional pharmaceutical formats like capsules, sublingual sprays and transdermal patches increase adoption among new demographics. Precisely dosed, standardised Extracts in these familiar formats also reassure prescribing clinicians. As patient feedback loops strengthen, we can expect even more tailored solutions that cater to specific patient needs and preferences.

Like mature markets in the US and Canada, advancements in cannabis extracts have shifted the market from primarily flower to extracted products like vapes and edibles, now comprising 40% flower and 60% extracts. Education and availability of in-demand products spurred this shift. European and global markets are poised for a similar transition as improved products at competitive pricing help patients and doctors discover optimal treatments. We are already seeing new pricing dynamics create demand, alongside the emergence of vaporizers, better-tasting preparations, resin extracts, and preferred delivery methods beyond traditional MCT oil drops. Faster-absorbing standardized products common in North America are entering Europe. These trends will likely drive a dramatic global market shift, as consumers move away from rolled flower towards more advanced product formats.

Michael Sassano,
Somai Pharmaceuticals Scaled GMP Manufacturing

The enhancement of EU-GMP certified production facilities signifies the industry's commitment to meeting the escalating patient demand with quality and consistency. The move towards standardisation through extract-based CBPMs will also pave the way for more rigorous data collection, further establishing their safety and efficacy.

At Grow we are seeing strong expansion in the medical cannabis market, particularly over the past twelve months. UK patients are overwhelmingly consuming flower but we are experiencing increasing demand in other segments, particularly in the vape category. We expect our product mix to continue to broaden next year, in-line with EU-GMP extraction and manufacturing capacity coming online in 2024. Many of our patients are searching for flower alternatives and we look forward to offering them some more innovative product formats in the year ahead. We are strong believers that manufacturing and R&D innovation will continue to be a key driver of medical cannabis adoption.

Dean Gainsley,
Grow Group Innovation and Differentiation

The industry is witnessing a surge in innovative techniques, such as nano emulsification, which offer enhanced pharmacokinetic profiles. The introduction of first-in-class formats, like rapid effect tablets, further broadens product differentiation. Leading producers are leveraging technological advancements from mature markets to manufacture high-quality CBPMs, ensuring that European operators remain at the forefront of innovation.

Panaxia is firmly committed to the principle that medical cannabis should be administered through precise and safe methods, such as oral consumption or inhalation via extracts, like inhalers. Patients should not be exposed to the uncertainties of smoking flowers, which may include undesirable elements like waxes and chlorophyll that can potentially harm them. Our recommendation is clear: opt for purified cannabis extracts designed for inhalation, containing only cannabinoids and terpenes, rigorously tested and proven safe for inhalation. Patients deserve nothing less.

We believe that within the next two years, the landscape of the German and Polish cannabis markets will undergo a significant transformation. We anticipate that over 35% of patients in these markets will make the switch from cannabis flowers to cannabis extracts. This shift underscores the growing recognition of the advantages offered by extracts, aligning with our commitment to delivering safer and more effective medical cannabis solutions.

Assi Rotbart,
Panaxia Favourable Demographic Trends

Anticipated growth in the over-65 demographic across EU countries unveils a vast potential for targeted medical and wellness solutions. This demographic, often suffering from chronic conditions, stands to benefit immensely from cannabinoid therapies. With an aging population, demand for alternative and effective treatments could surge, positioning CBPMs as a preferred choice for many.

In summary, the extracts sector stands at the cusp of transforming how CBPMs meld with contemporary pharmaceutical practices. Expansion is expected to be driven by maturing regulations, validation from clinicians, diverse CBPM offerings, enhanced EU-GMP production capabilities, and a steadfast dedication to the patient experience.

Appendix

European Requirements

Producing extract-based CBPMs for medical and pharmaceutical markets in Europe mandates strict adherence to regulatory standards. An overview of the key requirements is outlined below.

EU-GMP – Extractors aiming to engage in this field must secure EU-GMP (Good Manufacturing Practice) certification as either an Active Pharmaceutical Ingredient (API) or herbal medicine manufacturer. This necessitates the establishment of comprehensive standard operating procedures covering record-keeping, sanitation, equipment handling, labelling, and error reduction.

EU-GMP encompasses all facets of production and is subject to audit and certification by regulatory agencies within the respective facility's jurisdiction. It operates proactively to ensure consistent adherence to quality standards throughout the manufacturing process, minimising inherent risks. EU-GMP regulates various aspects, spanning input materials, premises, equipment, storage, record keeping, staff training, hygiene, complaint handling, and product development.

Compliance involves suitable equipment use, batch testing for initial outputs, and the establishment of continuous testing protocols. Upholding elevated standards, employing proficient staff, and robust production monitoring are imperative to ensure product purity and quality.

Narcotics Licences – Additionally, companies must possess the necessary licences to handle and produce pharmaceutical-grade CBPMs.

API Certification – API certification entails registration with health authorities. European companies can obtain a Certificate of Suitability (CEP) from the European Directorate for the Quality of Medicines and Healthcare (EDQM) or opt for certification through the Active Substance Master File (ASMF) procedure. In the US, a Type II Drug Master File (DMF) application is necessary for certification through the Food and Drug Administration (FDA).

ISO Standards – Parallelly, ISO (International Organisation for Standardisation) certifications, although aligned with GMP standards, predominantly concentrate on business and management systems. The ISO 9001 standard for Quality Management Systems is particularly compatible with GMP certification for extraction.

Import and Export – The cross-border movement of CBPMs within the EU poses unique challenges. A 2018 resolution encouraged the European Commission to embark on a harmonisation process for the legal framework of medical cannabis products across member states. While non-binding, this resolution steers the Commission's actions toward harmonisation. This ongoing process focuses initially on patient access and product standards. The absence of explicit plans for free trade in medical cannabis within the EU necessitates rigorous compliance with export and import regulations. Valid export permits and licences for import are prerequisites for the cross-border distribution of CBPMs.

Marketing Authorisations – Some countries with medical cannabis programs, such as Portugal and Denmark, have established marketing authorisation processes as an alternative approval pathway for CBPMs rather than requiring full pharmaceutical market authorisation.

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