

Successful Marketing of Medicinal Cannabis and Cannabis-derived Products – Part II

Abstract

In June, the first part of this article was published, describing differences in the legal background of some of the European Union countries, which need to be known for successful marketing. The second part of the article describes hurdles and requirements regarding growing, import and distribution of medicinal cannabis or cannabis-derived products, as well as the potential of this market concerning development of finished medicinal products as a next step of product development in this evolving market segment.

Keywords: medicinal cannabis, Cannabidiol, GMP, GDP, GACP, safety, efficacy, clinical data

Import of Medicinal Cannabis – More Complex than Expected

With the implementation of the Cannabis Law in Germany and Germany being the biggest European market for these medicinal products, the country was flooded with an overwhelming interest of cannabis-cultivating companies from abroad, mainly from non-EU countries on importing cannabis to Germany/EU, securing market shares as early as possible. In many cases the processes were investor-driven with the idea of quick business in Europe, but reality was slower. A lot of companies failed to see the pitfalls, based on missing knowledge on the broad legal background on medicinal products in general and on medicinal cannabis in particular, especially with its different national requirements by different European countries. It took quite a while to find a path through the legal and regulatory jungle on narcotic drugs and their exemptions, including such requirements as the establishment of qualified persons for narcotic drugs, wholesale licenses, GACP, GMP, underlying QM systems, import licences and radiation protection ordinance for marketing approval of irradiated cannabis. By now this path became a road with “mainly” clear directions for all stakeholders. New stakeholders on the market were in the

beginning not aware of the significant and pivotal role of “legal and regulatory affairs” for medicinal cannabis, which was necessary for a successful implementation of products for marketing approval. Every strategic decision of a company should be based on deep knowledge of national legal and regulatory requirements to turn a marketing strategy into a success. In addition, in such a regulated market as the one for medicinal cannabis, it is of intrinsic importance to find the right partnerships for all steps, from cultivation, storage, import, product analysis and release in the European country as well as delivery to the pharmacy at the very end. For new stakeholders it was extremely important to find supporting companies, being able to search for partners on any level in this very specialised area by using their network.

GMP / GPP – What’s the Difference?

Opening the German market for medicinal cannabis in 2017 led to huge interest from cannabis-cultivating companies from outside of the European Union. In contrast to their expectations, import to Europe in general or Germany more specifically was a complex path of regulatory requirements from different authorities.

Strong quality control underlies production of any medicinal product; the same is true for cultivation and harvest of medicinal cannabis, reflected by compliance to Good Agricultural and Collection Practice (GACP) and compliance to Good Manufacturing Practice (GMP).

Companies from outside of the European Union were confronted with the European requirements to cultivate and harvest cannabis according to Good Agricultural and Collection Practice (GACP) and to possess a certificate on Good Manufacturing Practice (GMP) issued by the concerned supervising authority. The first companies entering the European market were Canadian companies, who presented their licence on “Good Production Process” (GPP) – issued by Canada Health, based on the Canadian Cannabis Act reflecting compliance to the Good Production Practices (GPP) requirements of the Cannabis Regulations.

What is the difference between Canadian GPP and European GMP? Canadian GPP describes requirements for production of cannabis herb but covers only parts of the European GMP processes and their requirements, like standard operating procedures (SOPs), sanitation programmes, recall procedures. GMP has additional requirements, such as staff qualification and additional testing for stability, pesticides and others.

With reference to Eudralex Volume 4, Good Manufacturing Practice, Part II, European GMP is bindingly applicable with physical processing of the plants. The distinct processing steps from which the GMP requirements have to be met depends on the final product which is intended for the application in patients. All steps during cultivation, advancing this GMP-starting definition must show compliance with Good Agricultural and Collection Practice (GACP). The basis of GMP-compliance is the understanding of the whole production process regarding potential risk to product quality and patient safety. Setup of quality risk management, including measuring control steps and activities reducing these risks is an important requirement. A company’s GMP certificate is one of the most important prerequisites for receiving an import licence of medicinal cannabis to a country of the European Union.

Cannabis-based Medicinal Products on the Market – Current Situation in the European Union and in Germany

Within the European Union, the German medicinal cannabis market is the biggest. Due to this circumstance we focus on this market in the following.

According to the German legislation, social insurance code 5, article 31 subarticle 6, the following medicinal products are legally on the market in Germany: Sativex, Epidiolex, Canemes, Nabilon, Dronabinol, cannabis flos and cannabis extracts. Cannabis flos (flowers), extracts of cannabis and Dronabinol are delivered to the patient based on a patient’s individual prescription. These products are produced by the pharmacist as magistral formulations. Sativex®, Epidiolex and Canemes® are

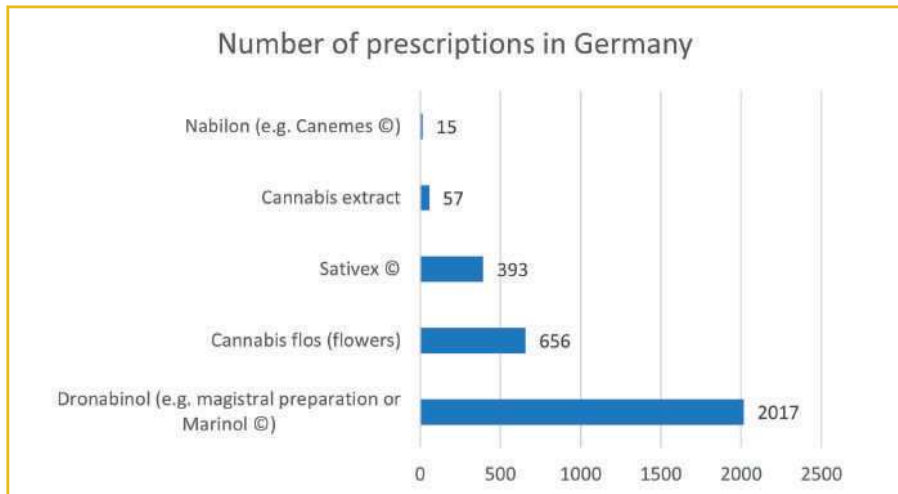


Fig. 1: Medicinal cannabis products and the number of prescriptions per product (data from Germany, 2019¹⁷)

finished medicinal product, delivered to the patient, in the pharmacy, off the shelf without any additional manufacturing step in the pharmacy. Finished product hereby means that these products are approved by competent authorities, confirming a positive benefit to risk ratio concerning efficacy and safety of the product, with data that has been derived from pre-clinical and clinical studies.

The German Authority (BfArM) analysed the prescription situation¹ for magistral formulations and finished products in Germany regarding the indication chronic pain (Fig. 1). The result shows a ranking of the number for prescriptions and products in decreasing order: Dronabinol, cannabis flos, Sativex, cannabis extracts and Nabilon (Canemes®) (Dr Cremer-Scheffer,

Symposium Medicinal Cannabis, Frankfurt, November 2019; status of data is March 2019).

Numbers on sales show a similar picture for product scaling. Data on sales between September 2018 and September 2019 was published in December 2019 by the German social health insurance information service (GAMSI, 2019, see Fig. 2), indicating that sales of medicinal cannabis² increased during the year, while sales of Sativex are more or less on a constant level. In April 2019, Germany introduced additional Retax-groups for cannabis-pharmacy products, leading to a change from three groups originally to five retax-groups³.

An analysis on availability of cannabis-based medicinal products in the EU

was conducted by several authors with the result that Sativex (Nabiximol, GW Pharmaceuticals) is available in most of the European countries, while Dronabinol and Nabilone are only available in a third of all EU countries^{4,5,6}. The latest product, which just received a European-wide marketing authorisation by the European Medicines Agency (EMA) in September 2019, is Epidiolex for treatment of patients, aged two years and older, who suffer from Lennox-Gastaut syndrome or Dravet syndrome and rare types of epilepsy that begin in childhood and can continue into adulthood. It contains Cannabidiol (CBD) as active substance.

Future Potential of the Medicinal Cannabis Market

Marketing medicinal cannabis products is strictly legally regulated throughout Europe and the market is highly competitive. As can be seen by the short overview on different national legislation in European countries (Part 1 of this publication) and implemented during the last years, the European market is highly diversely regulated. Companies planning the import of cannabis from outside of the EU, being unfamiliar with the different legal background directing marketing opportunities, are confronted with this complex situation. Sound and extensive expert knowledge is necessary to understand the national requirements, not to lose time to market.

A keyword for the basis of the diverse national legislation is for sure “missing data on safety and efficacy” to which the different countries react by using different strategies regarding patients’ safety. Opening the doors for medicinal cannabis was an answer to the need of patients being without alternatives in treatment, e.g. regarding chronic pain or during chemotherapeutic treatment. For sure cannabinoids are effective in treatment of certain disorders, but pre-clinical and clinical data is still missing for different indications for which medicinal cannabis is used today.

The clinical trial library “ClinicalTrials.gov”, provided by the U.S. National Library of Medicine, lists about 900 trials conducted with cannabis or cannabis-related substances as drug substance. Just to mention some of the different indications, there are 53 trials concerning cancer using either cannabis or cannabis-based medicinal products as drug substance, 10 trials on epilepsy, 29 on multiple sclerosis, 13 trials on insomnia,

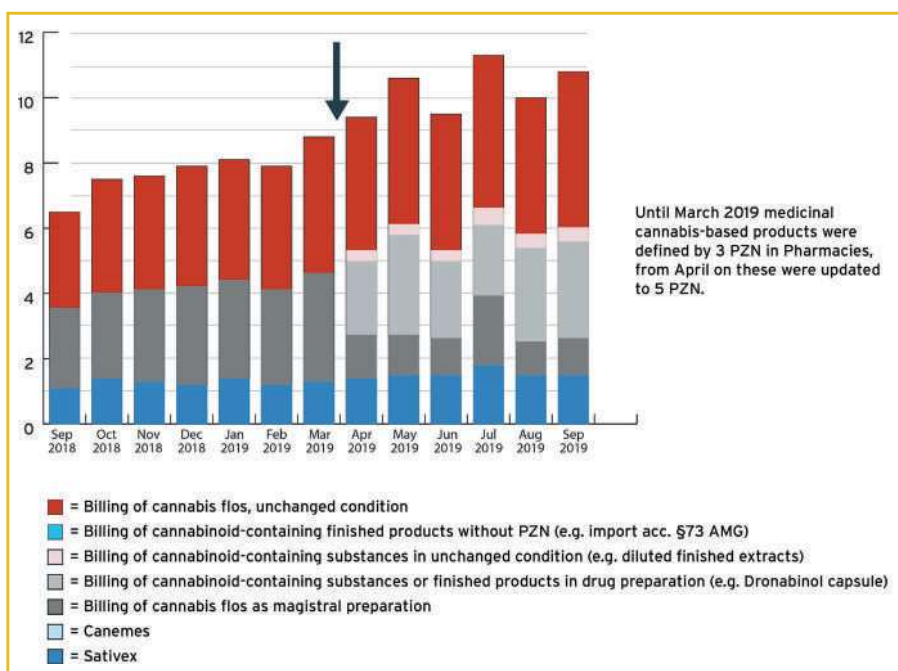


Fig. 2: Monthly gross profit of cannabinoid-containing finished products and magistral preparations [turnover in mio €], published by the German Social Insurance Information Service (GAMSI, 2019).

36 trials on stress, one trial on appetite disorder, five trials on dementia, one clinical trial on neuroprotection, 32 trials on chronic pain, 14 trials on drug addiction, 14 trials on attention deficit, 49 trials on schizophrenia, 35 trials on depression, one trial on Alzheimer's disease, three trials on osteoarthritis and two trials on psoriasis.

Up to now only a few cannabinoid prescription medicinal products were developed, e.g. Sativex and Epidiolex. Filling the lack of clinical data with results on toxicology, safety and efficacy in specific indications will strongly raise the interest of pharmaceutical companies in developing new products. This in turn will enlarge the market potential of cannabinoid-based medicinal products on prescription and will raise overall trust in the cannabis-based products and therapies. Clinical data might probably also help to distinguish responder-patients, who benefit from medicinal cannabis-based products in dosage form of inflorescences and tinctures, from non-responders, needing indication-specific cannabinoid prescription medicines.

With this vision in mind, it becomes quite clear that the market for medicinal cannabis

is not just a market bubble but a true new developing pharmaceutical area with a broad field of applications.

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