

Legal approaches for application of cannabis-based preparations in Europe

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Introduction

The medical use of cannabis-based preparations has a long tradition. It can refer to a wide range of preparations that contain a variety of substances contained in the plant *Cannabis* spp. The ratio of the active components varies in different strains of cannabis. Many of the substances have been isolated during the years, and after their characterization, the two that got the most attention in clinical studies are tetrahydrocannabinol (Δ^9 -THC), which has psychoactive properties, and cannabidiol (CBD), that has no psychoactive properties (Devinsky et al., 2014). Under international drug control treaties, cannabis use in Europe is limited to scientific and medical purposes, monitored by the national agencies responsible for controlling the production and supply of cannabis for medical use, while implementing various regulatory frameworks. The use of cannabis for medical purposes is justified only in case when there is evidence of the quality, safety and efficacy of the preparations for the corresponding indication. Many EU countries now allow the medical use of cannabis or cannabinoids in certain forms. Different approaches are used in different countries, leading to emerging of key issues that are challenges in the process of implementing cannabis preparations in medical practice (Bifulco and Pisanti, 2015).

The main purpose of this overview is evaluation of the regulations and practices for implementation of drugs that contain cannabinoids and cannabis-based preparations in Europe in medical practice, the regulatory requirements, the establishment of regulatory frameworks in specific countries of Europe, and forming the basis for upgrading of the national regulations on medical use of cannabis.

Materials and methods

Review of relevant European, US and Macedonian legislation, with particular attention to the Directives, regulations and guidelines from various legal bodies, and sources such as PubMed, Medline and other relevant websites with empirical analysis articles, which assess the impact of European and non-European Regulatory activities, diversity of the approaches that are currently being taken, and the importance of further investigating and advancement of the medical evidence for use of cannabis-based preparations in Europe.

Results and discussion

New policy approaches to medical cannabis use on other continents have prompted some European countries to allow patients to use cannabinoid-containing drugs and cannabis-based preparations under specific circumstances. European drug regulation is based on a network of 50 drug regulatory authorities in 31 European Economic Area (EEA) countries. In Europe, no standard regulatory framework has been developed for cannabis and cannabinoid products and there are significant variations between the approaches taken in Europe, reflecting various historical and cultural factors. In most countries, the supply of cannabis and cannabis-based preparations for medical use has evolved over time, often in response to product demand or product changes, and continues to change rapidly in the recent years. Some of the laws can be applied automatically and uniformly to all EU member states, while others need to be transposed into national legislation.

The medical use of cannabis and cannabinoids refers

to the application of the cannabis preparations for various medical conditions, with the aim to alleviate specific symptoms of some indications. They can contain different active substances and can be used in different administration routes. Cannabinoids may be derived from plants or synthesized in laboratory. For obtaining marketing authorization for any drug, including the drugs containing cannabinoids, the responsible authorities and manufacturers should control the safety, efficacy and evaluate the risk-benefit ratio of the drug, while the manufacturers are required to present evidence obtained from controlled clinical trials for use of the drug for the indication for which an application for marketing authorization has been submitted. Internationally, United Nations Substance Abuse Treaties, under which the medical use of cannabis is severely restricted, provide the background for regulatory frameworks for the medical use of these preparations in all signatory countries. In addition, at EU level, the EMA is responsible for the scientific evaluation, surveillance and monitoring of medicines, and coordinates a network of national regulatory authorities. Few countries that have developed systems for the legal production and distribution of cannabis for medical purposes are implementing legal measures to ensure that they are strictly regulated (EMCDDA, 2018).

Cannabis intended for medical use is cultivated and traded only under the supervision of the competent authorities, and all preparations containing psychoactive components of cannabis must be issued only with a licensed doctor's prescription, only in cases where there is evidence of their quality, safety and efficacy for the specific indication. (NASEM, 2017).

Several medicines containing cannabinoids for medical use are now allowed in many EU countries. The EU also has directives and regulations that apply to low-THC cannabis products in order to ensure their efficacy and safety, but since the preparations contain the non-psychoactive component CBD and the quantity of the psychotropic component THC is under specific, defined level, they are classified as food or dietary supplements and their issuing is not supervised. The results of several randomized controlled clinical trials on use of drugs that contain cannabinoids and cannabis-based preparations show that they alleviate the symptoms of some diseases. These preparations are used for symptomatic treatment, as a concomitant therapy to other medical treatments approved for certain indications. Some preparations based on cannabis for medical use have passed the regulatory process for obtaining marketing authorization, with data from clinical studies that confirm their efficacy and safety. Cannabinoid-containing drugs that have obtained marketing authorizations are: Epidiolex (cannabidiol), and 3 synthetic cannabis - containing medicines: Marinol

(dronabinol), Syndros (dronabinol) and Cesamet (nabilone). Except the drugs that contain cannabinoids that have obtained marketing authorization, some countries allow the patients access to standardized cannabis-based preparations for medical purposes, and the framework that evaluates the medical justification and allows the patients' access is closely monitored and regulated on national level in every country (EMCDDA, 2018).

Conclusion

The growing acceptance of potential treatment choices that has derived from cannabis in many countries can ease and set the regulatory pathway for relevant clinical trials that may demonstrate possible medical evidences for the effectiveness of cannabis preparations for a variety of indications. There are still open questions regarding the legal approaches of individual countries to cannabis, which would be resolved through a scientific evaluation of the impact of current legislation. Further discussions on changes and new implementations in legislation on medical use and cannabis supply across Europe will provide an objective and reliable basis for future decisions, with the primary aim of providing safe and effective drugs to patients.

References

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