

Approaches for regulation of the “off- label use” within the European Union

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Introduction

The European Medicines Agency defines the off-label use as "*situations where a medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information*". In other words, off-label use can be defined as the use of an authorized medicine in an unauthorized manner, which raises many questions about the risk, ethics and legality of this type of practice.

Studies show that about 40% of medicines in adults and up to 90% in children are used off-label (Gazarian et al., 2006). Some groups of patients are most affected, such as children, mental patients, cancer patients and patients with rare diseases where there is simply no alternative treatment with available authorized medicinal products (Weda et al., 2017).

Despite increasingly stringent regulations, off-label use remains a weak point in today's pharmaceutical legislation. In recent years, guidelines and legal changes in some countries have defined conditions and responsibilities, but in most European countries there are still no rules for off-label use (Drenska and Getov, 2017).

The purpose of this study is to identify and analyze different off-label regulatory approaches adopted by some Member States and to summarize efforts to establish a common harmonized approach

to regulate this practice within the European Union (EU).

Materials and methods

The subject of our research was Bulgaria and selected European countries (France, Italy, Spain, Germany and the United Kingdom), which have specific solutions to regulate this practice. Studied and analyzed were legal documents, manuals, expert opinions, scientific publications and other available information in PubMed, Google Scholar and Google, without limits in the time range.

Results and discussion

From all the countries studied, only in Bulgaria there are no clear rules for the off-label use of medicines. The measures taken by the other selected EU countries, are showing significant differences and a specific approach. Some are within the scope of pharmaceutical legislation, others within the national health insurance legislation, and some are guidelines of national medical associations.

The approaches taken by the United Kingdom and Spain give to doctors some freedom to use medicines off-label, but in certain conditions (lack of alternative treatment and / or informed consent from the patient).

In Italy, France and Germany, another approach has been taken. The off-label use is only allowed if

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they have gone through a specific approval procedure and the lists of medicines that can be used off-label are maintained by the relevant national medicine agencies.

Explicit informed consent from the patient is required in two of the countries - Spain and Italy, and in the United Kingdom, according to the prescribing guidelines, is advisable.

The analysis shows that, different approaches taken by these EU Member States have their advantages and disadvantages.

However, we found the approach in Spain to be the most comprehensive and effective, with the following arguments:

- Gives freedom to doctors in their work;
- Makes it possible to treat patients in urgent need;
- The fundamental right of the patient to be informed and to participate in treatment is guaranteed;
- Allows doctors to avoid liability associated with the off-label use;
- Protects authorized and clinically proven medicinal products;
- Ensures proper use and reduces risk.

Conclusion

The regulation of off-label use is highly recommended. The lack of rules for off-label use leads to uncertainty among doctors and to patient dissatisfaction. The presence of rules, facilitates patient access to medicines, increases the number of medicines doctors have and addresses many of the problematic aspects associated to this practice (e.g. safety, ethics, legality, etc.).

Finding a common solution for regulation of the off-label use across the EU, would harmonize the different approaches in different countries, but also would help others to impose control on this problematic practice.

References

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