Macedonian pharmaceutical bulletin, 68 (Suppl 1) 517 - 518 (2022)
Online ISSN 1857 - 8969
DOI:10.33320/maced.pharm.bull.2022.68.03.248
Short communication

"Skinny labelling" pathway: an instrument for circumventing second medical use patents by generic companies

Marija Mitkovska[1*], Aleksandra Krstevska[1], Dijana Nechkova[1], Katerina Anchevska Netkovska[2], Ana Poceva Panovska[2]

[1]*Alkaloid AD Skopje, Blvd. Aleksandar Makedonski 12, 1000 Skopje, Republic of North Macedonia*
[2]*Faculty of Pharmacy, Ss. Cyril and Methodius University, 1000 Skopje, Republic of North Macedonia*

Introduction

Discovering a new therapeutic indication of already known, and most probably, patented drugs is a common practice of originator companies. The incentive for repurposing of known drugs is their eligibility for an additional patent protection via so called second or further medical use patents (Burrichter et al., 2020). Besides to new therapeutic indication of known drugs, medical use patents, also refer to use of previously known indication but for a new patient group, a new dosage form or a new dosage regime.

Generally, the purpose of the second medical use patents is to postpone entering of generic drugs on market (Schandl, 2017). In order to avoid such market delays, generic companies can obtain market approval by a pathway called "carving-out" or "skinny labelling". This pathway allows generics to seek a market approval only for the unpatented medical uses of the originator drug, instead of waiting a patent expiration or attempting a patent invalidation (Walsh, 2021).

The purpose of this article is to show whether the "skinny labelling" pathway is sufficient instrument for circumventing second medical use patents in different jurisdictions within European Union (EU).

Materials and methods

A selection of an antidiabetic (a SGLT2 inhibitor) was made using the patent tool Ark Patent Intelligence. A patent research for its compound patent, their extensions and medical use patents was performed within European countries using the patent tools Patsnap and EPO. An analysis of the medical use patents in regards of the Public Assessment Report (PAR) of the antidiabetic was obtained.

Results and discussion

According to Article 11 of Directive 2001/83/EC (Directorate-General for Health and Food Safety, 2001), the European medicines legislation allows generic applicants to carve-out parts from the product information (Summary of Product Characteristics; SmPC) referring to indications or dosage forms which are protected by patent law in order to obtain a market approval before the patent expiration (England and Osgerby, 2013).

However, even though "skinny labeling" is allowed by European legislation, it has still a great legal uncertainty within European countries. This is so, because the infringement of patents according to Article 64(3) of European Patent Convention (EPC) is a national issue (EPO, 2020) and, thus, it does not fall under centralized rules of the EPC (Schandl, 2017). Nevertheless, prescribing or dispensing the drug for the labeled use may lead to indirect infringement of the medical use patents (Mahn, 2010). Additionally, since the prescription of off-label use became a practice recently, this act leads to direct patent infringement as well (Schandl, 2017).

For example, in Germany, generic companies are facing an increased risk of being liable for direct infringement of second medical use patents, even if they carve-out the patented therapeutic indications. The courts might still rule on infringement if a considerable amount of cross-label use can be proven (Burrichter et al., 2020). On the other hand, Dutch authority had a practice of publishing the full labeled version of the SmPC for a medicinal product, instead of the carved-out one. This

*mnikova@alkaloid.com.mk

practice has jeopardized the legal certainty and transparency for the healthcare professionals and patients making them liable for indirect patent infringement (Harford and Mulryne, 2019). In Italy, carving-out a patented indication from the SmPC does not alone save the generic companies from patent infringement. Generic companies also have to notify all relevant parties involved in the purchase and use of the product that the product should not be used for the patented indication (Amollini, 2022).

The compound patent of the selected antidiabetic, the SGLT2 inhibitor, should be valid until March 2025 in most of the European countries. A supplementary protection certificate (SPC) to the compound patent was granted and is expected to be valid until May 2029.

The antidiabetic was approved for the first time in Europe in May 2014 for improving glycemic control in adults with type 2 diabetes mellitus. In 2017 a variation proposing new therapeutic indication was submitted. The new indication, reducing the risk of cardiovascular events in adults with type 2 diabetes mellitus, was supported by new clinical data. The proposed therapeutic indication was not approved by European Medicine Agency (EMA) as a new indication, rather the first approved indication was modified in use of the antidiabetic in treatment of type 2 diabetes mellitus. However, in May 2021, a new therapeutic indication, use of the antidiabetic for treatment of heart failure, was approved by EMA.

Furthermore, two medical use patent applications have been filed in 2014 and 2017, separately. The one filed in 2014 is claiming use of the antidiabetic for reducing the risk of cardiovascular events in adults with type 2 diabetes mellitus, and the other patent application filed in 2017 is claiming use of the antidiabetic for treatment of heart failure. The first medical use patent application has fulfilled the patentability requirements and is expected to be granted. The second medical use patent application is still being prosecuted by European Patent Office (EPO). It is worth mentioning that both patent applications have been filed before the two therapeutic indications were approved by EMA.

In case patents to the medical use patent applications are going to be granted, the therapeutic indication treatment of type 2 diabetes mellitus should be modified in improving glycemic control in adults with type 2 diabetes mellitus and treatment of heart failure has to be carved-out from the SmPC in the generic applications for market approval (England, Osgerby, 2013). It is arguable whether the modification of the therapeutic indication could be allowed by European medicines legislation (Human Medicines Division, 2022). On the other hand, the deletion of the patent protected therapeutic indication may still lead generic companies to uncertainty for a patent infringement liability (Schandl, 2017).

Conclusion

Skinny labeling practice is inconsistent within EU countries. EU national patent systems should synchronize their approach when assessing patentability on second medical use inventions. A strictly defined rules on infringement liability of generic companies, practitioners, pharmacies and patients have to be implemented in the national patent systems in order to balance the patient needs from one side and the originators investments on the other side.

Implementing rules within European medicines legislation on providing clear information line, from generics product information, through practitioners and pharmacies, to patients as end point consumers, in order to control the cross- and off-label use of the patented therapeutic indications is necessary. Providing clear information by generics in market approval applications regarding valid medical use patents and their publication in the official drug registers of the regulatory agencies could be a step forward in avoiding direct and indirect patent infringement.

References

Ampollini, D., 2022. Skinny Label Insufficient for Avoiding Infringement of Second Medical Use Claims, says the Court of Mylan

Burrichter, A., Kirchhofer, N., Lödige, M., 2020. Second medical

use claims in pharmaceutical patents – sharp sword or toothless tiger?

Directorate-General for Health and Food Safety, 2001. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, Article 11.

England, P., Osgerby, K., 2013. Carve-outs and skinny labeling European Patent Office (EPO), 2020. Convention on the Grant of European Patents (European Patent Convention), Article 64.

Harford, K., Mulryne, J., 2019. CJEU Decision on Scope of Skinny Labels

Human Medicines Division, 2022. Coordination Group for Mutual Recognition and Decentralized Procedures – Human (CMDh), pp. 14: CMDh Minutes January 2022 - FOR PUBLICATION (hma.eu)

Mahn, G.T., 2010. Skinny Labeling and the Inducement of Patent Infringement

Schandl, C., 2017. Skinny Labeling and (Indirect) Infringement of Second Medical Use Patents in Europe, pp. 5, 9 - 11

Walsh, B., 2021. Skinny Labeling: “A Pathway for Timely Generic Drug Competition: https://doi.org/10.26099/b1c0-wn80