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Short communication

Medical use patents of antineoplastics: new trend of 'evergreening' and prevention generics on the market

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Introduction

Patents are legal instruments intended to encourage innovation by providing time limited exclusive rights to the inventor and to benefit a financial reward in the marketplace. The value of a patent portfolio stems from the ability to use the portfolio as a barrier that prevents others from making, using, importing, or selling similar products and/or providing similar services. The ability to prevent others from reaching a particular market is especially relevant for technology industries and business models where the only other barriers to market entry are often time and money.

Since patents rights have a limited validity period, 'evergreening' is the best tool for extended market monopoly, and it is a recent trend in the patent system, especially in pharmaceutical sector. Originators generally do ever-greening, by filing new patent application for existing molecules to show novelty (Jain, 2021). The second medical use patents are the main tool in the evergreening business strategy in oncology (Bansal and Sahu, 2009). Directly or indirectly, it creates monopolies which result in patent abuse affection the human rights (Lucose, 2016). The balance between the patent owner's interest and society is significant.

The focus in this article would be the medical use patents as a new trend of 'evergreening' in oncology.

Materials and methods

For the purpose of this study, three different antineoplastic drugs have been selected using the patent searching database Ark Patent Intelligence. A patent search for the medical use patents of the selected drugs have been conducted using the following patent searching databases: PatSnap, Espacenet and EPO. The patent analysis has been obtained within European countries in the meaning of European Patent Convention (EPC) and comparison of Public Assessment Reports (PAR) of originator's products.

Results and discussion

For a long period of time, the second medical use patents were considered as not patentable in Europe, contrary to first medical uses of a known product, which were patentable if they were complying with the patentability standards. The Munich Convention of 1973 rejected the patentability of second medical uses, because they were assimilated to a method of medical treatment, which was considered to lack industrial application. The European Patent Office (EPO) in the EPC amendments that entered into force in 2007 opens the door to the patentability of second medical uses (Ducimetière, 2019).

The second medical use patent in Europe is patentable only in form of Swiss claims, otherwise it will be excluded from patentability under Art. 53 (c) EPC (EPC, 2020). According to Guide for examination of EPO, the medical use patents could only be patented if their claims are in the form "Use of product X for the manufacture of a medicament for the therapeutic application Z", (Guidelines for examination in the EPO, 2022). The tendency for using medical use patents to prevent generics on the market, especially in oncology raises the question of whether those patents deviate from the ethical and moral norm, whether they are patentable under art.53 (a) EPC (Krichhfer, 2020).

On the other hand, European Medicine Agency (EMA) has implemented regulations regarding the medical use patents and registrations of generic drugs. According EMA regulations the patented indications can be deleted from sections 4.1. therapeutic indications, 4.2. posology and method administration and 5.1. pharmacodynamic properties of the Summary of Product Characteristics (SmPC). EMA through those regulations

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facilitates the entry of generic drugs on the market (EMA, 2021).

Due to the awareness of this strategies, originators are referring to indirect infringement of their patent rights through prescription of the drugs for the patented indications. In this case, many medicinal practitioners are required to prescribe the drug by the trademark (Kilpatrick, 2019). How the trend of evergreening through medical use patents influences generic market launch in oncology would be presented through the analysis of the examples below.

First antineoplastic that would be analyzed is Celgene's antineoplastic. The compound patent has expired, however, there is a valid Supplementary Protection Certificate (SPC) until 2022. Within the period of validity of the compound patent protection, Celgene has filed a patent application in 2003 for use of the antineoplastic for treatment of myelodysplastic syndrome. Additionally, in 2007 they filed a patent application for treatment of mantle cell lymphoma. With this patent strategy Celgene enjoys a monopoly on the market for 30 years, and takes all the financial benefits from it. The only way for generics to market the product is to carve-out those indications.

The compound patent of Bristol-Myers Squibb's antineoplastic has been revoked after opposition proceedings at EPO. They also filed applications for SPC and pediatric extension, which if were valid would prolong the monopoly of the compound patent for another two years. Since this strategy was not successful, they tried to prevent generics on the market using the medical use patent as a barrier. There is a patent claiming the use of the compound for treatment of chronic myelogenous leukemia valid until 2024. In order to have early launch, generics would market the product without this indication, but the risk of indirect infringement is still there. With good business strategy and intellectual property knowledge the generics companies would have a good chance to remove that barrier.

Another example of 'evergreening' trend is BTG's prostate cancer drug. The compound patent and SPC have expired in 2018. Also, there is an existing patent claiming the use of the drug in combination with corticosteroid valid until 2027. Although in the initial patent analysis, the patent document may be identified as a patent claiming method of treatment and fixed-dose combination product, with comprehensive analysis of the PAR of this antineoplastic, it is clear that the originator drug is used only in combination with corticosteroid, and this patent document is also critical for generics launches. At the moment, the medical use patent is under opposition proceedings at EPO. If the final decision of EPO is invalidation of the patent, the date of earliest launch will be defined by other aspects. Since this is the main indication and the generics must have the same method of administration as a reference drug, this patent is crucial for generics business strategies, whether they will wait for EPO decision or they will launch the product with the risk of infringement. The extended originators monopoly for an average of 28 years for the mentioned drugs, shows the real situation that many generic companies are facing, the unfair practices which are broadly followed by originators to preserve the financial benefit.

Although according to EMA regulations the generic companies could register the product with curve-out of patented indication, the risk of legal disputes is still present, since the indirect infringement of the medical use patents could be done by medical practitioners.

Conclusion

With patenting the second medical use of known compounds, originator's monopoly is extended for compounds that are already a prior art. If so far, the main purpose of patents was scientific progress, the 'evergreening' trend shows the aspiration of originators for economic advantages. Since there is a risk of indirect infringement, we assume that only major generic companies would take the risk to market products with non-patented therapeutic indications.

In Europe where second medical use patents are allowed, we propose that stricter patentability standards should be applied when assessing their inventive contribution. Additionally, national laws should clearly determine the bounds of originator's monopoly position. Hence, in order to launch their products without infringing originator's patent rights, generic companies should indicate clearly in their patent information leaflets and SmPCs, the non-patented therapeutic indications for which the drugs could only be prescribed by practitioners.

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