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Short communication

Global Marketing Authorization: A field of frequent legal disputes and its benefits to generic companies

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Introduction

Marketing authorization (MA) is a procedure which ensures quality, safety and efficacy of pharmaceutical products. Originator companies are therefore compensated for their investment in new products, as well as their innovation through periods of data and market exclusivity. (European Commission, 2019).

Here are several ways in which an originator company can "strategically" extend drugs' market exclusivity (orphan status, pediatric extension, new therapeutic indication, etc.), prolonging the entry of a more available, generic product on the market. For that purpose, there are few measures for preventing monopoly-"global marketing authorization" (GMA) being one of them. GMA is a regulatory concept which is defined by Article 6(1) of Directive 2001/83/EC, according to which *"when a medicinal product has been granted an initial marketing authorization, any additional strengths, pharmaceutical forms, administration routes, presentations as well as any variations and extensions shall be considered as belonging to the same global marketing authorization in particular for the purposes of the application of Article 10(1), generic application"*. This concept applies to products authorized by the same marketing authorization holder (MAH), to all products regardless to their registration date (European Commission, 2019). Main focus of this article is to give a critical overview of the concept of GMA from two different perspectives: on one hand, with regards to the legislation set up in Directive 2001/83/EC and on the other, to review the implications of this concept on the generic drug industry.

Materials and methods

An antipsychotic was selected by using the patent-searching tool PatSnap. The displayed information was reviewed using publicly accessible information such as Public Assessment Reports (PARs) retrieved from following medicinal product databases: European Medicine Agency (EMA), Community Register of centrally authorized products and Mutual Recognition Information (MRI).

Results and discussion

According to Article 10(1) of Directive 2001/83/EC, generic products authorized without providing the results of pre-clinical and clinical trials, must not be placed on the market until ten years (data and market exclusivity) have expired from the initial authorization of the reference product. This ten-year period can only be prolonged for one additional year of protection in the case of authorized new indications, with significant clinical benefit. To capitalize from the additional year, the new indication must be approved during the first eight years since the initial MA has been granted.

In addition, according to Article 6(1) of the same Directive, after granting of the initial MA, every variation should be included in the said authorization or GMA (unless it is proven they significantly differ in safety/efficacy).

This means that for a reference medicinal product, the periods of data and market exclusivity begin from the date when the first MA is granted. All additional variations and extensions have the same end dates as the initial product, regardless to their date of MA (Article 6(1) of Directive 2001/83/EC).

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Since products falling within the scope of GMA are not clearly distinguished, it is difficult for EMA to exhibit consistent judgement, and therefore companies often have opposing views, making it a field, susceptible to frequent legal disputes (European Commission, 2019).

The selected antipsychotic is a product that clearly displays the intent of this concept. The originator first registered this drug as tablets in 2007, for the treatment of schizophrenia and psychotic disorders. In 2011, the originator obtained another MA for the same drug as prolonged release suspension for monthly injection used for the maintenance treatment of schizophrenia in adults. In 2014, the originator registered a third product with the same drug as a 3-monthly injection, indicated for the maintenance treatment of schizophrenia in adult patients. Since, the company referred to data from the drug registered in 2011 to support the use of the antipsychotic as 3-monthly injection, no new data protection period would apply for the third product (Directorate-General for Health and Food Safety, 2001).

On the other hand, the second product has separate MA and does not fall within the scope of GMA, since the originator submitted results of new pre-clinical and clinical trials. Furthermore, they did not cross-refer to data from the first product (tablets), considering that the two products differ in terms of efficacy, safety, and pharmacokinetics profile.

The court practice shows that generic companies are frequently the subject of further legal disputes, even when relying on the concept of GMA covered by Article 6(1) of Directive 2001/83/EC.

In court case no. T-472/12, the originator obtained a MA for new indications just by modifying the dose, for a medicinal product that already had valid MA. After expiry of the protection period of the initial product (indicated for the treatment of bone complications in patients with cancer), a generic company filed an application for a generic version of the second registered product (indicated for the treatment of osteoporosis in men and women who have been through menopause, as well as Paget's disease in adults), relying to the GMA concept. However, the originator challenged the granted generic MA before the General Court of the EU, claiming that both products did not fall within the same GMA.

The General Court rejected the appeals of the originator, ruling that both products were included in the same GMA (Carías, 2017). This decision is in line with the GMA concept, considering that under Article 6(1) of Directive 2001/83/EC it is generally not possible to secure a new period of data and market exclusivity for a new therapeutic indication, for an active substance that is already the subject of an MA held by the same MA holder (Faircliffle, 2015).

In a recent case (no. T-611/18), the General Court annulled the decision of EMA not to accept a generic application for MA. In 2006, Biogen acquires a company that holds the MA of a product containing dimethyl and monoethyl fumarate salts, indicated for psoriasis. A few years later Biogen files an application for MA for a medicinal product containing only dimethyl fumarate for the treatment of multiple sclerosis which EMA approves. Later on, a generic company disputes EMA's decision to grant a MA to Biogen and the General Court agrees with that statement, making EMA's decision not to put the new indication in GMA invalid (Den Boer, 2021). Biogen could only get additional one year of market protection for new indication, no new set of data and market protection. To sum up, in this case, even if the General Court made a right verdict to nullify EMA's decision, the procedure took valuable time from generic companies by which they could have marketed their products.

Conclusion

Even though there are Directives governing the registration of products, set by the regulatory agencies in Europe (Articles 10(1) and 6(1) of Directive 2001/83/EC), the legal practice shows that there are frequent conflicts between originators attempting to preserve their status on the market and generics trying to launch their generic counterpart. This indicates that even if generics applying for MA refer to the concept of GMA, they still might be legally disputed from originator companies. Procedures like such, take up both time and valuable resources from both parties. To prevent this, EMA should make consistent decisions regarding granting of new MA according to the abovementioned directives. However, the fact that majority of the cases are in the favor of generic companies serves as an incentive for other generics to dispute wrongfully obtained MAs, enabling them to launch products that are more available to the general public.

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