BIOBETTERS AS ALTERNATIVES TO BIOSIMILARS FOR INCREASING ACCESSIBILITY TO BIOLOGIC DRUGS

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Introduction

Biologics are expensive drugs, and such high costs push the public health system budget and may impair access of patients to such increasingly important drugs (SILVA; GUERRA, 2019). Despite representing only about 2% of all drugs purchased, biologic drugs comprise 40% of the pharmaceutical assistance budget of the Brazilian Ministry of Health (VIEIRA, 2018). The introduction of biosimilar drugs has been shown to allow a reduction in the average purchase cost of biologic drugs, increasing accessibility thereto (TAVEIRA, RAQUEL, 2019). However, there are still barriers to biosimilars, including regulatory requirements and third parties' intellectual property rights (VERMA; JAIN; CHAUHAN, 2018). As biosimilar developers grow closer to gaining approval for and launching their products, innovator biologic developers are taking on new strategies. The high complexity of biological medicines has given rise to innovations applied or based on known products, and from there, new biological medicines have emerged, which are only unofficially called biobetters (KUMAR; CHAWLA; DUTTA, 2018). Biobetters may potentially mitigate some of the risks associated with the introduction of biosimilars in the market. Since, as opposed to biosimilars, biobetters are supposed to be innovative and improved products compared to the reference products, they may take advantage of strategies available for overcoming patent and regulatory-related barriers, they may avoid the necessity of awaiting the expiration of third parties' patent rights (ROYZMAN; COHEN, [s.d.]). Accordingly, the present work aims to address the hypothesis that biobetter drugs can be alternatives over biosimilars in order to increase quality, safety and innovation of healthcare products, while decreasing prices, making biologic drugs more accessible, and overcoming market barriers such as third parties' intellectual property rights and competitor products, as well as doctor and patient's acceptance.

Method

This study is limited to biologic drugs listed on RENAME section L (immunomodulators and antineoplastic agents). The biologic drugs listed on RENAME section L were individually searched in the "active principle" field of ANVISA database for registered drugs and blood derivates]. A patent search was performed in the database of the National Institute of Industrial Property (INPI), using keywords for each drug, such as biologic target (e.g. CTLA-4, TNF-α IL-6), disease or condition treated, (e.g. inflammation, cancer, viral infection) drug type (e.g. antibody, fusion protein, interferon). All retrieved patents and patent applications were individually evaluated with regard to their administrative status, i.e. pending or non-pending patent application, valid or non-valid patents, as well as to their subject matters (i.e. molecules, pharmaceutical formulations, processes and second medical uses).

Results / Discussion

The estimated validity term of patents derived and yet pending patent applications (if granted) were estimated. The results indicated that only monoclonal antibodies and the HG-CSF analog filgrastim are

currently under patent protection: 5 of the 10 monoclonal antibodies (adalimimabe, basiliximabe, daclizumabe, eculizumabe and rituximabe) are currently under public domain. The HG-CSF analog filgrastim will only be under public domain after 2028. The results also suggest that no further opportunities for biosimilars will be open until 2027, when the patent for ustequinumabe expires. In 2028, the patents for infliximab and filgrastim will expire after 27 and 28 years, respectively, due to exceptional provisions of the Brazilian Industrial Property Law 9,279, of May 14, 1997 ("L9279", [s.d.]). Such special provision is the Sole Paragraph of Article 40, which provides that a patent of invention shall not be valid for less than 10 years after the granting date. Accordingly, patents in Brazil may be an even greater barrier to biosimilar developers than in other countries. Although no definitive regulatory pathway for biobetters exists, there are still significant advantages of following a biobetter route for approval. Knowing the target biology and clinical background for enabling efficacy in a disease can reduce the risks associated with drug development (BURCHIEL; ASPBURY; MUNDAY, 2019). The regulatory process for biobetters tend to be longer and more expensive, as such drugs are currently seen as new drugs. On the other hand, unlike biobetters, biosimilars are normally impaired by patent rights ("Biosimilars and Biobetters Offer Unique Benefits and Risks", 2015) which may put the marketing of such products on hold for decades.

Conclusion

Alternative and less expensive biologic drug therapies are needed. Biobetters and Biosimilars also have the potential to reduce healthcare costs. Unlike biosimilars, biobetters are not faced with the burden of having to be similar to the originator biologic. This frees companies to use more modern and potentially less costly manufacturing methods. In addition, as a better or more convenient medicine, having more convenient administration route or regimen, improved efficacy or safety, biobetters offer a marketing advantage over the originator biologic or its biosimilars. Biobetters have the potential to offer tremendous commercial advantages over originator or biosimilar drugs, as well as to receive patent protection and market exclusivity. The findings of this study show that biobetter drugs can be alternatives over biosimilars in order to increase quality, safety and innovation of healthcare products, while decreasing prices, making biologic drugs more accessible, and overcoming market barriers such as third parties' intellectual property rights and competitor products, as well as doctor and patient's acceptance.

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