Chelonian Conservation And Biology

Vol. 17No.2 (2022) | https://www.acgpublishing.com/ | ISSN - 1071-8443

DOI:doi.org/10.18011/2022.04(1) 1333.1340

THE EFFICACY OF BIOPHARMACEUTICALS IN DISEASE MANAGEMENT

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Abstract

Biopharmaceutical medications, which were first introduced in 1982, have significantly transformed the treatment of a wide range of disorders and are now being used in almost every field of medicine. The biopharmaceuticals market has had rapid expansion in recent years, surpassing the overall medicine market. It is expected to continue growing dynamically because to the high demand for these treatments. Biobetters, which consist of modified active pharmaceutical components that exhibit improved effectiveness, will have a significant impact on the advancement of biopharmaceuticals. Biosimilars are another important category of biopharmaceuticals. Their entry into the European Union and, more recently, the United States markets will result in decreased costs for biopharmaceutical therapy. This study focuses on the latest advancements in the area of biopharmaceutical research and the challenges related to the approval of novel biopharmaceuticals and biosimilars. This text discusses the primary category of biopharmaceuticals, the present state of the biopharmaceuticals market, and predictions for the future.

Keywords: biopharmaceuticals, disease management, biosimilars, drug market, challenges.

1. Biopharmaceuticals

Biopharmaceuticals exemplify the most notable achievements of contemporary scientific advancements. These medications are now widely used in almost every field of medicine and have emerged as very successful therapeutic approaches for a wide array of conditions, such as malignancies and metabolic disorders. The term "biopharmaceuticals" was created in the 1980s to describe medications that are manufactured utilizing molecular biology technologies in biotechnological procedures. Therefore, this specific set of goods was differentiated from the larger classification of biologics, which are medications manufactured using traditional biological techniques. 1,2

Biopharmaceuticals provide several benefits. They selectively target particular molecules, resulting in minimal side effects often associated with traditional small-molecule medicines. Furthermore, as compared to traditional medications, biopharmaceuticals demonstrate a notable

level of specificity and efficacy. 3. Biopharmaceuticals have improved the treatment of individuals who have a limited response to conventional synthetic medications.

2. Biopharmaceuticals and synthetic medicines

Biopharmaceuticals are distinct from synthetic medications in every aspect. The distinctions between these two classifications of medications include several aspects such as the characteristics of the product, the origin of the active ingredient, the requirements for bioequivalence, the identification, structure, manufacturing techniques, composition, dosage, formulation, handling, intellectual property rights, legal restrictions, and marketing. 1.

Biopharmaceuticals are manufactured using live cells, whereas synthetic medications are created by chemical procedures. The majority of synthetic medications consist of tiny molecules. As an example, a single molecule of acetylsalicylic acid consists of a total of 21 atoms. On the other hand, biopharmaceuticals are often 100-1000 times bigger in size 4. The active pharmacological component of such a medication may consist of a range of 2000 to 25,000 atoms. Biopharmaceuticals have a higher level of structural complexity due to the presence of polymeric chains that display significant variations in their structure.

Verifying the purity of the active component in a pharmaceutical medicine and the composition of the final product may be done with relative ease. Chemical compounds that are very pure and obtained from different sources, particularly those that consist of a combination of isomers, might be regarded as comparable or even identical for practical purposes. 1. Biopharmaceuticals provide a distinct scenario. Due to the biological disparities in the expression systems and the manufacturing process settings, there may be some level of variability, even across multiple batches of the same product. 5. Consequently, it is necessary to monitor changes across batches in order to assure compliance within a defined range. The characteristics of active medicinal components in biopharmaceuticals, apart from their core structure (such as the sequence of amino acids), are greatly influenced by the production process. Hence, it is postulated that the result of biopharmaceuticals is determined by the process itself.

Biopharmaceuticals have certain features that set them apart from synthetic medications, such as their susceptibility to breakdown in the digestive system and their restricted capacity to pass past the intestinal epithelium 8. Consequently, they are usually given by direct injection into the body rather than being taken orally. Biopharmaceuticals need intricate stabilizing systems due to their susceptibility to temperature variations. Biopharmaceuticals possess far more intricate mechanisms of action compared to manufactured medications. Interferon has a significant impact on the expression of about 40 genes. The intricate nature of these medications frequently poses challenges in fully understanding their mechanisms of action. 9.

Furthermore, unlike synthetic medications, biopharmaceuticals have the potential to induce an immune response. Slight variations in the composition of the active component may have a

significant impact on the drug's ability to stimulate an immune response. Immunogenicity may also be caused by contaminants associated to the process.13,14

3. Comparison between generics and biosimilars

Generics are pharmaceutical products that are identical to the original reference medications in terms of their active medicinal component. The word pertains to alternatives for synthetic medications. Due to the specific attributes of these medications, it is generally quick, easy, and cost-effective to produce a formulation that contains an identical replica of the active medicinal component. Based on the statistics from the American Federal Trade Commission, the process of developing a generic medication typically takes 3-5 years and incurs a cost ranging from $1-5 million. Moreover, a generic version of the medicine may cost 80-90% less than the original reference drug 16.

The word "generic" is not applicable to biopharmaceuticals. The European Medicines Agency (EMA) has determined that the word "biosimilars" should be used in the European Union (EU) to designate biological medical goods that include a version of the active pharmaceutical component present in previously authorized reference biological medicinal products 17, 18. The phrase "follow-on biologics" is used by the U.S. Food and Drug Administration (FDA). Furthermore, both of these organizations concluded that biosimilars may exhibit distinct mechanisms of action compared to the reference medicine 19, 20.

The variations come from the use of distinct expression systems and diverse manufacturing and purifying procedures in the biosimilar manufacture. It is impossible to create an exact replica of any biopharmaceutical, even if the methods used to produce it are the same, such as using mammalian cells or bacteria. Biosimilars may possibly exhibit variations in their glycosylation pattern or the electrical potential of the active pharmacological component compared to the new reference medications. These disparities may impact the efficacy, potency, and security of the medication 21, 22. Consequently, the pharmacokinetic and pharmacodynamic characteristics of biosimilars and reference biopharmaceuticals may also vary. Advancements in bioproduction and analytical techniques have enabled the production of proteins and glycoproteins that closely resemble the reference product 23.

4. Biosimilars and generics registration

The distinction between biosimilars and generics has an impact on the processes for registering biosimilars. The registration standards for biosimilars are less demanding than those for new biopharmaceuticals but harsher than those for generics. Biosimilars are approved for registration based on their established resemblance to the matching, previously registered novel medication. These drugs may be registered either after submitting the necessary paperwork, which includes comparing them to the reference medication, or after submitting comprehensive documentation, similar to what is needed for a novel drug.24,25

The European recommendations 17 were established in 2005, and a comparable set of rules was published in the United States 24 in 2010. The first biosimilar, somatotropin (known as Omnitrope), was officially approved in the European Union in 2006. Currently, the European Union (EU) has registered a total of 23 biosimilars with the European Medicines Agency (EMA). These include five erythropoietins (EPO) used for treating anemia caused by dialysis and chemotherapy, seven filgrastim-granulocyte colony stimulating factors (G-CSF) used for treating leucopenia caused by chemotherapy, one human growth hormone used for treating growth disorders, two folliculotropic hormones used for treating fertility disorders, two insulin glargine, two enoxaparin sodium - an anticoagulant used for preventing blood clots, and four antibodies, including infliximab and etanercept. Monoclonal antibodies are anticipated to be the next wave of biosimilars. The first biosimilar monoclonal antibody, infliximab, was officially approved in the European Union in 2013. Infliximab is a monoclonal antibody that specifically targets tumor necrosis factor (TNF), and it is used in the treatment of autoimmune conditions, including rheumatoid arthritis and Crohn's disease. The medicine was registered as two separate products, Inflectra and Remsima, since one business produces the active pharmacological substance, which is then turned into the finished drug by two different manufacturers. 26

The FDA authorized the first biosimilar, filgrastim-sndz (brand name Zarxio), in March 2015 in the United States. Zarxio, a biosimilar of filgrastim (brand name Neupogen), is made by the European business Sandoz. The initial development and production of filgrastim was done by Amgen Inc. Zarxio is indicated for the treatment of the same medical disorders as Neupogen 27. However, it received approval as a biosimilar rather than a direct replacement.

5. Biopharmaceutical production systems

Biopharmaceuticals differ from synthetic medications in that they consist of recombinant proteins and nucleic acids as their active pharmaceutical components. At present, most biopharmaceuticals that are available for purchase comprise recombinant proteins as their main active component. These proteins are synthesized in prokaryotic systems, primarily *Escherichia coli*, or eukaryotic systems using fungi such as Saccharomyces cerevisiae and Pichia pastoris, mammalian cells, or insect cell lines. Research has also investigated the use of cell-free expression systems (in vitro systems), which substantially simplify the modification of synthesis conditions.

Each of the listed approaches for producing biopharmaceuticals has its own benefits and disadvantages. Various expression techniques are used for recombinant proteins depending on their distinct features.

6. Monoclonal antibodies

Monoclonal antibodies (mAbs) are the predominant category of biopharmaceuticals and are now used in the treatment of cancer, inflammatory illnesses, cardiovascular diseases, organ transplantations, infections, respiratory diseases, and ophthalmologic diseases. This category of

biopharmaceuticals includes monoclonal antibodies (mAbs) and modified versions of antibodies, such as bispecific antibodies (bsAbs), antibody-drug conjugates, radiolabeled antibody conjugates, antigen-binding fragment Fab, and Fc-fusion proteins. 28,29

The presence of totally human and humanized monoclonal antibodies (mAbs) has significantly enhanced the effectiveness of treatments for oncology, hematooncology, as well as inflammatory and autoimmune illnesses. The first biopharmaceutical using monoclonal antibodies was muromonab-CD3, commercially known as Orthoclone OKT3. It is used in the treatment of acute kidney transplant rejection. The medicine was officially registered in 1986. However, significant advancements in the antibody market started in the late 1990s with the registration of the first chimeric monoclonal antibody (mAb). As of March 2017, a combined total of 71 monoclonal antibody-based medications have been registered in the European Union and the United States. At now, the percentage of totally human antibodies among monoclonal antibodies (mAbs) being used in medical clinics is increasing. The first entirely human monoclonal antibody, adalimumab, was authorized by the FDA in 2002. Since then, almost 40% of all the monoclonal antibodies (mAbs) that have been brought to market are of totally human origin.30

7. Conclusion

The biopharmaceutical market has had a more rapid growth rate compared to the overall medication industry in recent years. Analysts predict that this market will sustain its growth. The recent and expected upward trends in biopharmaceutical sales can be attributed, in part, to the expanding elderly population and the subsequent rise in chronic illnesses, the increasing prevalence of diabetes and cancer patients, and a higher occurrence of autoimmune diseases. Understanding the mechanisms behind different medical disorders has helped to identify particular elements and processes that cause the pathological alterations. This has sparked ongoing investigation into the suitability of biopharmaceuticals in novel clinical scenarios.

The established effectiveness of biopharmaceutical medications and their endorsement as therapeutic remedies by medical professionals and patients together contribute to the increasing demand for novel biopharmaceuticals. A benefit of its utilization is the provision of tailored remedies instead than symptomatic therapy 31.

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