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A Detailed Review On Biologics and Biosimilars

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Abstract –

Biologics and biosimilars have emerged as pivotal components of modern healthcare, offering innovative solutions to a wide range of diseases. This poster delves into the intricacies of these biological products, their development, regulatory frameworks, and their impact on the global healthcare. Biologics are a category of medications derived from living organisms, such as cells, tissues, or proteins, and are used to treat a wide range of diseases, especially those that cannot be addressed effectively by traditional small-molecule drugs. Unlike chemically synthesized drugs, biologics are made from complex biological sources like human or animal cells, bacteria, or yeast and Biosimilars are highly similar, but not identical, versions of biologics that have lost patent protection. Like generic versions of small-molecule drugs, biosimilars offer more affordable alternatives to biologics. Biological medicines (biologics) are produced in living cells and purified in complex, multi-step processes. Compared with chemically synthesized small-molecule drugs, biologics are more sensitive to changes in manufacturing conditions. Process and product consistency should be founded on rigorous design and control of manufacturing processes, but consistency is ultimately ensured through robust quality systems. Even a minor change in any component of a quality system could lead to product drift, evolution, and divergence, which may impact the quality, safety, efficacy, and/or interchangeability of biologics. The therapeutic success of biotechnological drugs, commonly designated as biologics, such as monoclonal antibodies (mAbs) and recombinant versions of endogenous proteins, is increasingly transforming the pharmaceutical market. Patent expiry of biologics (ie, originators) has also opened the field to the so-called biosimilars, medicines that are intended to be similar, although not identical, to the originator biologics in terms of quality, efficacy, and tolerability. It is undeniable that there are highly debated issues regarding biosimilars in immune-mediated inflammatory diseases: increasing demand for biologics given their clinical success, the nearing of patent expiry for the 4 top-selling biologic brands, and the search for reducing the economic burden of drugs.

Keywords – Biotechnology, Immunotherapy ,Drug development Regulatory approval, Safety and efficacy, Quality assurance, Innovation, Generic medications, interchangeability.

Introduction –

A biologic or biological product is a preparation, such as a therapeutic drug or a vaccine, made from living organisms, either human, animal, yeast, or microorganisms. Biologics are composed of proteins (and/or their constituent amino acids), carbohydrates (such as sugars), nucleic acids (such as DNA), or combinations of these substances. Biologics may also be cells or tissues used in transplantation. A biosimilar, sometimes referred to as a follow-on biologic, is a therapeutic drug that is similar but not structurally identical to the brand-name biologic made by a pharmaceutical or biotechnology company. The brand-name product is sometimes referred to as the innovator or reference product. Biopharmaceuticals, also called 'biological medicinal products' or 'biological medicines', are medicines whose active drug substance is made by a living organism or derived from a living organism by means of recombinant DNA and/or controlled gene expression methods. These products are polypeptides, glycoproteins, and/or nucleic acids and their molecular characteristics are much more complex than traditional chemical drugs.

Biologics are complex, large-molecule drugs derived from living organisms, including proteins, nucleic acids, or cells, used in the treatment, diagnosis, or prevention of diseases. They have revolutionized the management of various conditions, such as autoimmune diseases and cancers, by targeting specific components of the immune system or cancer cells.

Biosimilars are biologic medical products that are highly similar to an already FDA-approved biologic, known as the reference product. While not identical, biosimilars have no clinically meaningful differences in terms of safety, purity, and potency compared to their reference products. The development of biosimilars aims to increase treatment options and reduce healthcare costs by providing more affordable alternatives to existing biologics.

The approval process for biosimilars involves rigorous evaluation to ensure they meet high standards of safety and efficacy. Manufacturers must demonstrate that patients using biosimilars do not experience any new or worsening side effects compared to those taking the original biologics. This thorough evaluation ensures that biosimilars provide the same treatment benefits and have the same risks as the original biologic.

The Introduction of biosimilars has led to increased competition in the pharmaceutical market, resulting in substantial savings for patients and healthcare systems. For instance, the U.S. biosimilars market has seen significant growth since the first biosimilar approval in 2015, contributing to reduced costs and expanded access to essential therapies.

In summary, biologics and biosimilars represent significant advancements in medical treatments, offering effective options for various diseases. The development and approval of biosimilars provide more treatment choices and have the potential to lower healthcare costs while maintaining high standards of patient care.

Biologics and biosimilars represent two important categories in the pharmaceutical industry, particularly for the treatment of complex diseases like cancer, autoimmune disorders, and chronic conditions such as rheumatoid arthritis.

1.Biologics –

Biologics are large, complex molecules or mixtures of molecules that are typically produced using living cells. They include therapeutic proteins (like monoclonal antibodies), vaccines, and gene therapies. Biologics have revolutionized the treatment of many serious conditions, offering targeted therapies that can be highly effective and tailored to individual patients. Some well-known examples of biologics include Humira (adalimumab) for rheumatoid arthritis and Herceptin (trastuzumab) for breast cancer.

Advantages of Biologics:

Targeted treatments: Biologics can target specific molecules or cells involved in disease, offering more precision than traditional small-molecule drugs.

Effectiveness: Many biologics have shown high efficacy in treating diseases that were difficult to manage with older treatments.

Reduced side effects: As biologics tend to be more targeted, they often come with fewer side effects compared to traditional chemotherapy or other non-targeted drugs.

Challenges:

High cost: Biologics are expensive to develop and manufacture, which translates into high treatment costs for patients and healthcare systems.

Administration: Many biologics need to be injected or infused, which may be inconvenient for patients and require specialized healthcare settings.

Complexity: The production of biologics is highly complex and regulated, leading to manufacturing challenges and the need for strict oversight.

2 .Biosimilars:

Biosimilars are biologic medical products highly similar to an already approved reference biologic product. They are not exact replicas due to the complexity of biologic molecules but are close enough in structure, function, and efficacy. The approval of biosimilars offers a more affordable alternative to original biologics. Regulatory agencies like the U.S. FDA and the European Medicines Agency (EMA) have rigorous processes to ensure that biosimilars are safe and effective.

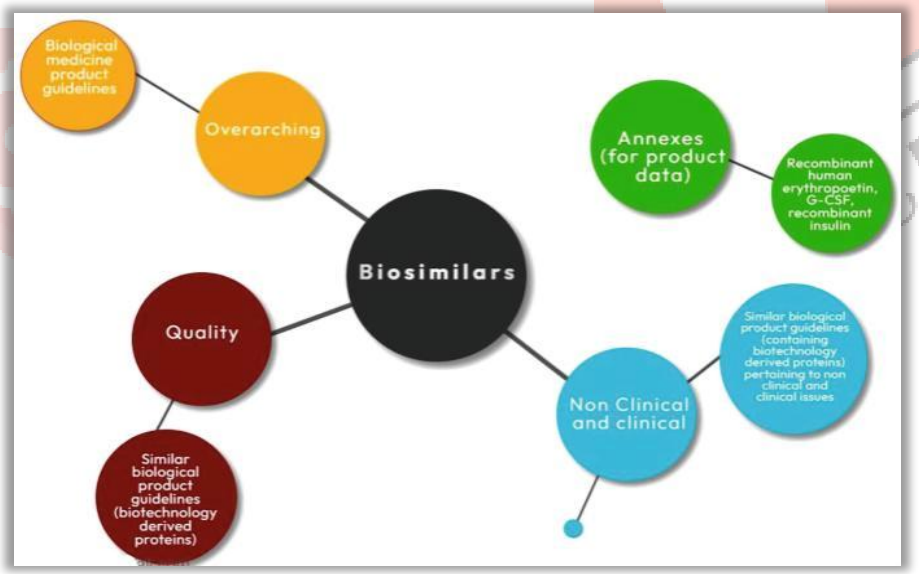

Fig 1 :Regulatory and Quality Considerations for Biosimilars Development

Advantages of Biosimilars:

Cost-effectiveness: Biosimilars are generally less expensive than their reference biologics, making them a more affordable option for patients and healthcare systems.

Increased access: Lower costs can lead to greater access to life-saving biologic therapies, especially in low- and middle-income countries.

Competition: The introduction of biosimilars into the market can drive competition, potentially leading to reduced prices for biologics.

Challenges:

Complexity in approval: While biosimilars are similar to their reference products, their development and approval are complex, requiring extensive clinical trials to demonstrate equivalency in terms of safety, efficacy, and immunogenicity.

Public and physician acceptance: Some healthcare professionals and patients are wary of switching to biosimilars due to concerns about potential differences in efficacy or side effects, despite regulatory assurances.

Interchangeability: Biosimilars may not always be interchangeable with the reference product, meaning that patients and doctors might have to make more informed choices about switching treatments.

Contents-

Structural and functional complexity of biologics-

Unlike single molecules which are chemically synthesised with highly predictable structures and functions, biologics are pharmaceutical compounds synthesised or extracted from a biological source often with highly complex structures. They can be broadly divided into monoclonal antibodies, receptor modulators or replacement/modulators of enzymes.2 The manufacturing processes of biologics involve living systems (eg, mammalian cell lines, microbial agents, plants, fungus) and complex processes (eg, gene isolation, recombinant DNA engineering, protein purification) which require high technological expertise with These compounds often have additional moieties, such as glycocarbohydrates, fatty acids and amino acids used to maintain the triple or quadruple structures. These high-molecular weight compounds require special formulations including stabilisers and preservatives for storage, which can influence their pharmacokinetic and pharmacodynamic properties, as well as their biological activities.

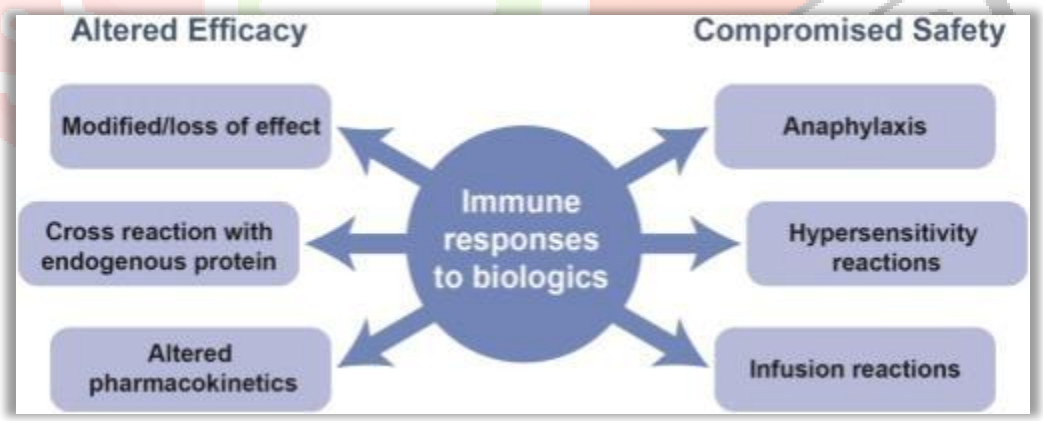

Fig 2 : Impact of Immune Responses to Biologics on Efficacy and Safety

Future of Biologics -

1.Personalized Medicine and Gene Therapies: The field of biologics will continue to evolve towards more personalized treatments, with an increasing focus on gene therapies and cell-based therapies. The development of biologics that target specific genetic mutations or individual biomarkers will lead to more effective, tailored treatments. For example, CAR-T therapies (Chimeric Antigen Receptor T-cell therapies) are already being used in oncology, and their expansion is expected in other disease areas.

2.Innovative Biologic Products: New biologic drug classes, such as bispecific antibodies and monoclonal antibody-drug conjugates (ADCs), will expand therapeutic options for diseases like cancer, autoimmune disorders, and rare diseases. These innovative biologics combine multiple mechanisms of action to improve efficacy and reduce side effects.

3.Combination Therapies: As the understanding of disease biology deepens, biologics are likely to be used in combination with other treatments (including other biologics, small molecules, and immunotherapies) to increase their effectiveness, particularly in complex diseases like cancer.

4.Manufacturing Advancements: Biologics production will become more efficient due to advances in biomanufacturing technologies, such as cell-free systems and improved bioreactor designs. These improvements can lower production costs and address scalability issues, making biologics more accessible globally.

Future of Biosimilars -

1.Increased Market Penetration: As more biosimilars are approved, particularly in large therapeutic classes like oncology, immunology, and endocrinology, the competition will likely drive down prices, increasing the accessibility of biologics to a broader population. More countries, including developing nations, will integrate biosimilars into their healthcare systems.

2.Interchangeability and Substitution: As regulatory frameworks evolve, biosimilars may become more widely interchangeable with their reference products. This interchangeability will ease the adoption of biosimilars by healthcare providers and patients, making the transition from reference biologics smoother.

3.Expanded Biosimilar Applications: In the coming years, we can expect biosimilars to be developed for a broader range of biologic drugs, including those that are currently under patent protection. The increased variety of biosimilars could further reduce treatment costs and promote more competitive markets.

4.Regulatory Frameworks and Education: As biosimilars become more prevalent, there will be an increased focus on regulatory standards, ensuring that biosimilars meet high safety and efficacy standards. Education campaigns aimed at healthcare providers and patients will be crucial to overcoming skepticism and promoting biosimilar adoption.

Applications –

1.Biosimilar

Biosimilars are biologic medical products that are highly similar to already approved reference biologic medicines, with no clinically meaningful differences in terms of safety, efficacy, and quality. Their applications include:

• Oncology: Used in the treatment of cancer, such as monoclonal antibodies (e.g., trastuzumab, rituximab) that target cancer cells.

• Autoimmune diseases: Such as rheumatoid arthritis, Crohn’s disease, and psoriasis, with biosimilars of TNF inhibitors like adalimumab and infliximab.

• Chronic diseases: Including diabetes (e.g., insulin) and growth disorders (e.g., growth hormone).

• Hematology: Used in the treatment of anemia related to chronic kidney disease (e.g., erythropoiesis-stimulating agents like epoetin alfa).

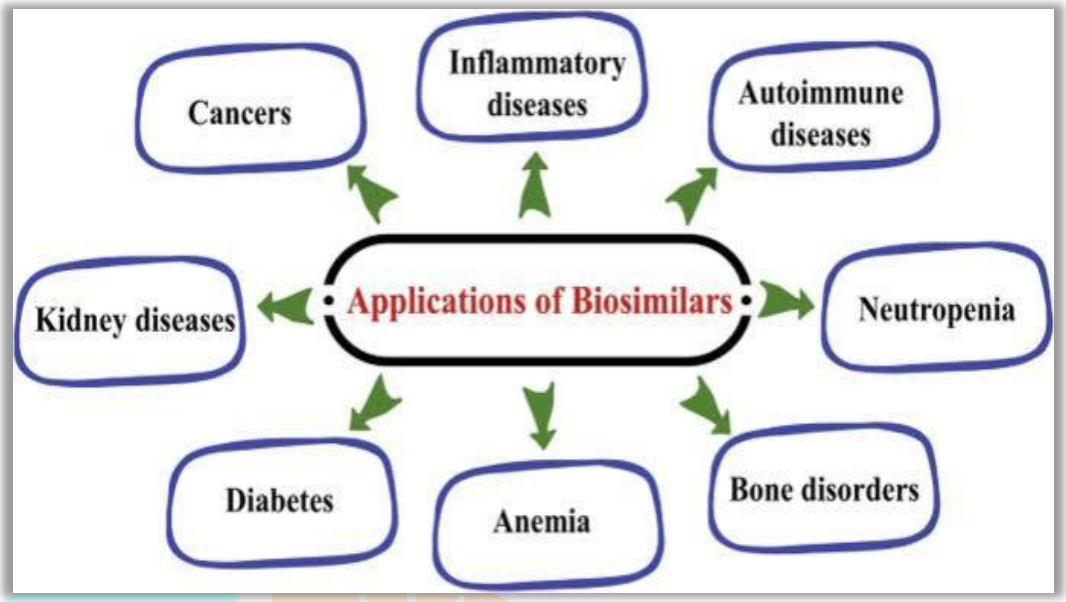

Fig 3: Applications of Biosimilars

2.Biologics –

Biologics are medicines derived from living organisms that include a wide variety of products like monoclonal antibodies, vaccines, gene therapies, and blood products. Applications include:

• Cancer treatment: Monoclonal antibodies (e.g., rituximab, trastuzumab) for targeting specific tumor markers.

• Immunotherapy: Biologics used to modulate the immune system for conditions like rheumatoid arthritis, lupus, and inflammatory bowel diseases.

• Infectious diseases: Vaccines (e.g., MRNA vaccines for COVID-19) and biologics targeting infections like HIV (e.g., antiretroviral therapies).

• Gene therapy: Biologics that are used for gene editing and introducing new genes to treat genetic disorders.

Economics of biosimilar and biologics –

1.Biosimilar –

• Definition: Biosimilars are biologic medical products highly similar to already approved reference biologics. They are not identical to the original biologic, but they have no clinically meaningful differences in terms of safety, effectiveness, and quality.

• Development Costs: Developing a biosimilar is less expensive than developing a new biologic because much of the initial research is already completed. The cost to develop a biosimilar is estimated to be about 30% lower than that of a new biologic.

• Pricing: Biosimilars are typically priced 15-35% lower than the reference biologic, which can lead to substantial savings for healthcare systems.

• Market Impact: The introduction of biosimilars increases competition in the biologic market, which can lower prices and improve patient access to these drugs.

2.Biologics –

• Definition: Biologics are large, complex molecules made from living cells, used in the treatment of a variety of diseases, including cancer, autoimmune disorders, and genetic conditions.

• Development Costs: Biologics have high development costs due to their complexity and lengthy clinical trial process. The cost of developing a biologic drug can exceed $1 billion, and these drugs can take 10-15 years to develop.

• Market Price: Biologics are often priced very high due to the high research and manufacturing costs. This leads to high healthcare spending.

• Patent Protection: Biologics are typically protected by patents for up to 20 years, and during this time, the company has exclusive rights to market the product.

Prescribing, dispensing and administering of biologics-

From a prescribing perspective, many doctors were trained to use generic names of the molecules, so-called international non-proprietary names. In many healthcare institutions, automatic substitution using generic drugs is often practised for cost control. Although this practice is widely accepted for single molecules, most regulatory agencies and learnt societies recommend documentation of product identity, brand name, manufacturer name and batch number of biologics. However, these changes in practices and nomenclatures require considerable education of the prescribers. Besides, system support is needed to establish product inventory for tracking and recall purpose, which may not be readily available in small practices and/or institutions, especially in developing countries.

Using biosimilars to increase access and reduce cost-

Despite the high cost of development, due to their targeted nature with high efficacy, biologics are now taking on an increasingly important role in the treatment of common and/or serious diseases such as diabetes, cancer, chronic kidney disease, rheumatoid arthritis, psoriasis, blood disorders, vaccines and inflammatory bowel diseases. In these diseases, proteins such as hormones, growth factors and inflammatory cytokines are disease mediators that form the basis for drug development. In 2016, more than 10 biologics were blockbuster drugs with annual revenue of billions of dollars. With anticipated patent expiry of many of these originator compounds, biosimilars are now given accelerated paths for development in order to increase market access and affordability of these compounds.

Current status –

Europe was the first in the world to formulate the policy framework for the approval of the biological product. The first biosimilar, Omnitrope (a recombinant human growth was), was approved in Europe by the European Medicines Agency (EMA) in 2006.United States followed this much later when in 2015 it approved filgrastim-sndz , a biosimilar to filgrastim (granulocyte CSF), whereas filgrastim was approved by the USFDA in 1991. But since then, FDA has approved a number of biosimilars for the treatment of cancer and other conditions. The latest one to be approved was pegfilgratism-jmdb in June 2018 to reduce the risk of infection following myelosuppressive chemotherapy . Now there are multiple biosimilars developed by biopharmaceutical companies and used across the world for wide range of areas such as diabetes, ophthalmology, and respiratory to cancer and connective tissue diseases.

India has a thriving biosimilar ecosystem in comparison to other countries and because of that Indian pharmaceutical companies have risen as the global market leaders in biosimilars. India approved its first biosimilar much before the United States and Europe. The first biosimilar was approved and marketed in India in 2000 for hepatitis B, although no specific guideline was available at that time for the development and marketing of biosimilar in India. Since then several biosimilars were developed and marketed in India by various biopharmaceutical companies. Recently, an Indian biopharmaceutical company got the USFDA's nod for marketing its novel biologic. Herceptin (active drug is trastuzumab) was the first biologic to be approved by FDA, which is used in certain breast and stomach cancer. This was also the first similar biologics manufactured by an Indian company, which received approval to market in the United States.

Conclusion –

Biosimilars hold promise to improve patient's accessibility for many malignant and nonmalignant ailments by reducing the treatment cost. Since the use of the □rst biosimilar, the development and uses of "biosimilars or similar biologics" have witnessed substantial growth.

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