INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

Biosimilar Drug: Current Situation

Jagruti Pansare*[1], Shraddha Bhalake[2], Sayali Erande[3], Ragini Patil[4]

[1,3,4]*Assistant Professor, Matoshri College of Pharmacy, Eklahare, Nashik*
[2]*Student, Dnyanvilas College of Pharmacy, Dudulgaon, Pimpari Chinchawad, Pune*

ARTICLE INFO

Published: 29 Nov. 2024
Keywords:
Biosimilar Drug, similar biologics, biologics requires careful clinical monitoring
DOI:
10.5281/zenodo.14246072

ABSTRACT

Biopharmaceuticals, derived from living cells through biological processes, replicate natural substances like hormones, offering targeted treatments for various diseases. As patents for original biologic drugs expire, biosimilars—subsequent versions of these drugs with similar but not identical characteristics—have emerged as cost-effective alternatives. In India, these are termed "similar biologics," with regulatory guidelines ensuring their safety, efficacy, and quality. Biosimilars are categorized based on their production processes, regulatory pathways, and branding strategies. Despite the promise of biosimilars in reducing healthcare costs and increasing patient access, their adoption has raised concerns, particularly regarding potential immunogenic reactions and treatment efficacy when switching from the original biologic to a biosimilar. New approvals for biologics in 2024, such as Epysli and Ahzantive, reflect the growth of the medical landscape and offer new treatments for conditions such as autoimmune diseases, eye disease, and cancer. However, the introduction of biologics requires careful clinical monitoring of safety and efficacy over time. The future of biosimilars is poised for growth due to patent expirations on many biologics and the development of new biologics. Access will increase if the doctor has adequate training, patient knowledge and insurance coverage. Regulatory frameworks must continue to evolve to meet the unique challenges of biologics development and ensure safety in clinical practice.

INTRODUCTION

Biopharmaceuticals are drug treatments derived from residing cells through organic processes, replicating herbal materials like hormones. Biosimilars are the next variations of unique biological tablets, already authorized for use, with comparable however no longer the same traits. In India, regulatory hints describe "comparable biologics" as bioengineered merchandise that declares equivalence in protection, efficacy, and pleasant to authorized reference biologics. Biosimilar medicines include a comparable

***Corresponding Author:** Jagruti Pansare
Address: *Assistant Professor, Matoshri College of Pharmacy, Eklahare, Nashik.*
Email ✉: pansarejagruti2402@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

energetic factor to the reference drug and are used to deal with equal situations on the same dosage. Biosimilars may be categorized into 3 categories: - Product- and process-primarily based totally - Regulated through abbreviated trying out - Marketed with the aid of using the equal producer beneath a distinct brand Pharmaceutical marketers referred to as biologics or healing proteins are synthesized in laboratories to duplicate the shape and characteristic of clearly taking place proteins withinside the human body. These lab-created proteins can both increase or inhibit the moves in their herbal counterparts. Produced through mobile systems, biologics have established powerful in treating numerous conditions, which include rheumatoid arthritis, ankylosing spondylitis, and inflammatory bowel diseases. Nevertheless, their excessive manufacturing fees impose a considerable burden on healthcare systems, restricting accessibility for lots patients.

The worldwide income of monoclonal antibody therapy, a form of biologic, is projected to reach $one hundred twenty-five billion with the aid of 2020. In reaction to the expiration of patents on biologic tablets, biosimilar tablets were advanced to cope with this challenge. According to the FDA, biosimilars are organic merchandise which might be tremendously much like their reference counterparts, without a clinically considerable variations. Although biosimilars are nonetheless produced the use of mobile systems, their improvement entails opposite engineering, because the unique synthesis pathways are the number one goals of biosimilar improvement are to lower healthcare spending on high priced biologic remedies and beautify affected person get right of entry to those important medicines. In 2013, the European Medicines Agency (EMA) authorized the primary biosimilars of infliximab (CT-P13). However, preliminary worries had been raised with the aid of using the European Crohn's and Colitis Organization concerning the adoption of biosimilars. A internet survey performed amongst corporation participants found out a lack of knowledge approximately the traits and packages of biosimilars, highlighting the want for schooling and awareness. To make sure the protection and efficacy of biosimilars, complete comparison research are important to verify that there aren't any considerable variations among the biosimilar and the reference product in phrases of potency, protection, purity, and effectiveness. The US FDA recognizes biosimilars as safe, powerful, and lower priced remedy alternatives for numerous clinical conditions, which include ankylosing spondylitis, inflammatory bowel disease, rheumatoid arthritis, plaque psoriasis, kind 1 diabetes mellitus, and unique sorts of cancer. As the biosimilars marketplace keeps to grow, there's an growing call for switching among distinct biosimilars (cross-switching) to optimize fitness outcomes.

List of New Biosimilar Medicines:

The biosimilar landscape has expanded with recent approvals, offering new therapeutic options for a variety of conditions. The main additions in 2024 are:

1**] Epysqli (eculizumab-aagh):** It was clarified in July 2024 for the treatment of rare blood diseases and autoimmune diseases.

2] **Ahzantive (aflibercept-mrbb):** approved in June 2024 for eye diseases such as age-related macular degeneration.

3**] Pyzchiva (ustekinumab-ttwe):** approved in June 2024 as an anti-inflammatory biologic.

4**] Nypozi (filgrastim-txid):** Approved in June 2024 as a biologic for Neupogen and corrects neutropenia.

5**} Bkemv (eculizumab-aeeb):** Approved as biosimilar to Soliris in May 2024.

6**] Yesafili (aflibercept-jbvf) and Opuviz (aflibercept-yszy)** : both were discharged in May 2024 due to eye problems.

7**] Hercessi (trastuzumab-strf):** approved in April 2024 as a biosimilar for Herceptin, used for the treatment of cancer.

8] **Selarsdi (ustekinumab-aekn):** Approved in April 2024 as a biosimilar option for Stelara.

9**] Tyruko (natalizumab-sztn):** approved in August 2023 for MS and expected to launch soon.

10**] Wyost (denosumab-bbdz)**: approved in March 2024 as the most effective cross-linking biosimilar to Xgeva and inhibits bone activity associated with cancer.

These new biologics will expand treatment options, potentially reduce costs and increase patient access..

The current Evidence:

In areas where biosimilars are accessible, biosimilar versions of tumor necrosis factor inhibitors (TNFIs) have become a common treatment choice for rheumatoid arthritis (RA) patients receiving biologic disease-modifying antirheumatic medications. When contemplating a treatment switch or substitution, healthcare providers must rely on the most robust and reliable evidence available. However, it is crucial to determine whether switching from a reference product to a biosimilar or undergoing multiple switches could impact treatment efficacy or compromise patient safety. Despite concerns about potential immunogenic reactions, reduced treatment effectiveness, and increased safety risks associated with switching, there is currently limited scientific evidence to either confirm or refute these concerns. A systematic review of studies examining the impact of switching between biologic and biosimilar versions of adalimumab, etanercept, and infliximab on RA treatment outcomes found no significant differences in efficacy, safety, or immunogenicity. The review noted that most studies involved a single switch from a reference product to a biologic, with only two studies examining the reverse switch. The evidence suggests that switching between biologics and biologics does not significantly affect treatment outcomes.

Pharmacovigilance And Biosimilar

"Pharmacovigilance plays an important role in the monitoring of biological drugs, because they are not the same to the reference products produced by different companies. "For this reason, unexpected side effects are only seen after extensive use of the biosimilar for a long time and in a large patient population.".

Future directions for biosimilars:

The future expiration of biosimilars patents will drive the development of new biosimilars and increase their availability. Currently, many biologics are used to treat inflammatory bowel disease and gastrointestinal cancers without biosimilars. The extent to which biologics are used depends on physician availability and patient education. Clinical studies and additional data increase a doctor's confidence. Better insurance coverage increases patient access to biologics. As more biologics enter the market, insurers are better equipped to cover new biologics. Features biologics approved for inflammatory bowel disease and cancer, including Crohn's disease, ulcerative colitis, colon and gastric cancer. This table also lists the FDA-approved biologics for each biologic. Biologics approved for the management of gastrointestinal inflammatory and oncological condition: -

Condition/Disease	Biologic	FDA Approved Biosimilar
Crohn’s Disease	Infliximab (Anti-TNF)	Flixabi Inflectra
Gastric Cancer	Trastuzumab (Anti-HER 2/new)	Ogivri
Colorectal Cancer	Cetuximab (Anti-EGFR)	An FDA appsroved biosimilar is not available.

Indian Guidelines:

Regulatory Framework for Biosimilars in India

In 2012, the Department of Biotechnology (DBT) introduced draft guidelines for similar biologics, outlining the regulatory requirements for marketing authorization in India. These guidelines ensure a comprehensive evaluation of biosimilars, including a comparability exercise, to guarantee their safety, efficacy, and quality. India's regulatory approach for biosimilars aligns with international standards, adopting a stepwise approach to approval. The Genetic Engineering Approval Committee (GEAC) and the Review Committee on Genetic Manipulation, in conjunction with the DCGI, oversee the approval of clinical trials for biosimilar products in India.

To obtain approval, biosimilars must demonstrate equivalence through rigorous non-clinical and clinical studies, including pharmacokinetics, toxicology, and efficacy assessments. India's biosimilar market encompasses a range of products, including vaccines, monoclonal antibodies, and recombinant proteins, with a detailed status report provided.

Fda Approach Regarding The Use Of Biosimilar Drugs

"The US Food and Drug Administration (FDA) has established a comprehensive framework for the approval and use of biosimilar drugs, aiming to ensure their safety, efficacy, and quality.

1. Stepwise approach: The FDA uses a stepwise approach to evaluate biosimilarity, starting with structural and functional characterization, followed by animal studies, and finally, clinical trials.

2. Comparability exercise: Biosimilars must demonstrate comparability to the reference product in terms of pharmacokinetics, pharmacodynamics, and immunogenicity.

3. Clinical trials: Biosimilars must undergo rigorous clinical trials to demonstrate efficacy, safety, and immunogenicity.

4. Interchangeability: The FDA has a separate pathway for designating biosimilars as interchangeable, allowing for automatic substitution at the pharmacy level.

5. Naming convention: The FDA requires biosimilars to have a unique name, including a suffix to distinguish them from the reference product.

6. Labeling requirements: Biosimilar labels must include information on the reference product, as well as any differences in dosing, administration, or safety.

7. post-marketing surveillance: The FDA monitors biosimilar safety and efficacy through post-marketing surveillance and adverse event reporting. By adopting this comprehensive approach, the FDA aims to ensure that biosimilar drugs are safe, effective, and of high quality, while also promoting competition and innovation in the biologics market."

Outcomes And Analysis:

A small change in the manufacturing process for epoetin (erythropoietin) can cause a serious disease, pure red cell aplasia, which shows the want to strengthen the law. In response, drug authorities created strict guidelines to ensure safety. Similarly, the European Medicines Agency (EMEA) and the Committee for Medicinal Products for Human Use (CHMP) raised concerns that Marvell insulin was not the same as human reference insulin, which led Marvel Life Sciences to Ltd. project due to failure to meet CHMP standards. Despite this, biosimilar insulin is still strong in the Indian market, showing the importance of legal and regulatory principles for biosimilars, different from those applicable generics.

CONCLUSION:

Biosimilars have the potential to improve patient access to prescription drugs as well as reduce financial pressure on healthcare systems worldwide. But to do this, doctors should make it

easier to prescribe biologic drugs instead of their reference products and pay for biologic drugs that are less expensive than their biologic counterparts. Biosimilars are not just inventions. Biologics are larger and more complex than chemical drugs, and because of the complexity of biological/biotechnology products, the scientific method for biosimilar products is not appropriate. To confirm biologics, well-designed clinical studies must be used. The challenge with biosimilars is understanding the differences that are clinically important. Current studies evaluating bio-disposal to biologics, investigating single-switch scenarios, show that these actions are generally safe and do not compromise e! cacy. . However, more research is needed to address specific areas such as long-term safety data requirements, different study models, and concerns about potential immunogenicity in multiple cross-sectional settings. Moving forward, there may be a better understanding of the global evidence for biosimilar cross-linking in various clinical settings as biosimilar technology develops. Ultimately, it guides clinical decisions about the best patient outcomes over the course of a year.

REFERENCES

1. Socinski MA, Curigliano G, Jacobs I, Gumbiner B, MacDonald J, Thomas D. Clinical considerations for the development of biosimilars in oncology. MAbs. 2015;7:286–293. [PMC free article] [PubMed] [Google Scholar]
2. Ecker DM, Jones SD, Levine HL. The therapeutic monoclonal antibody market. MAbs. 2015;7:9–14. [PMC free article] [PubMed] [Google Scholar]
3. Schellekens H, Moors E. Clinical comparability and European biosimilar regulations. Nat Biotechnol.2010;28:28–31. [PubMed] [Google Scholar]
4. Mellstedt H, Niederwieser D, Ludwig H. The challenge of biosimilars. Ann Oncol. 2008;19:411–419. [PubMed] [Google Scholar]
5. Kanters TA, Stevanovic J, Huys I, Vulto AG, Simoens S. Adoption of Biosimilar Infliximab for Rheumatoid Arthritis, Ankylosing Spondylitis, and Inflammatory Bowel Diseases in the EU5: A Budget Impact Analysis Using a Delphi Panel. Front Pharmacol. 2017;8:322.
6. Dranitsaris G, Amir E, Dorward K. Biosimilars of biological drug therapies: Regulatory, clinical and commercial considerations. Drugs. 2011;71:1527–36. [PubMed] [Google Scholar]
7. Crommelin DJ, Storm G, Verrijk R, de Leede L, Jiskoot W, Hennink WE. Shifting paradigms: Biopharmaceuticals versus low molecular weight drugs. Int J Pharm. 2003;266:3–16. [PubMed] [Google Scholar]
8. Brockmeyer C, Seidl A. Binocrit: assessment of quality, safety and efficacy of biopharmaceuticals. Eur J Hosp Pharm Pract. 2009;15:34–40. [Google Scholar
9. Schellekens H, Casadevall N. Immunogenicity of recombinant human proteins: Causes and consequences. J Neurol. 2004;251(Suppl 2):II4–9. [PubMed] [Google Scholar]
10. The New India Guidelines on Similar Biologics. 2012. Oct, [Last accessed on 2013 Jul 16]. Available from: http://www.biospectrumasia.com/biospectrum/analysis/3021/biosimilars-guidelines-a-step-directionindia#. UehBf6DRiSo .
11. Smeeding J, Malone DC, Ramchandani M, et al. Biosimilars: considerations for payers. P T. 2019 Jan;44(2):54–63. doi: 10.1056/NEJMp1107285 PubMed Google Scholar
12. ‘Generic’ biologic drugs appear comparable to brand-name counterparts. Johns Hopkins bloomberg school public health. 2016.

https://publichealth.jhu.edu/2016/generic-biologic-drugs-appearcomparable- to-brand-namecounterparts#:~: text=They%20took%20the%20data%20from ,e$ectiveness %20as%20their%20branded%20counterparts Google Scholar

13. NHS. Biosimilar medicines. England: NHS. https://www.england.nhs.uk/medicines-2/biosimilar-medicines/ Google Scholar
14. Kvien TK, Patel K, Strand V. The cost savings of biosimilars can help increase patient access and lift the "nancial burden of health care systems. Semin Arthritis Rheum. 2022;52:151939. doi:1016/j.semarthrit.2021.11.009 PubMed Web of Science ® Google Scholar
15. van der Plas RM, Hoefnagel MHN, Hillege HL, et al. Pragmatic rules for comparability of biological medicinal products. Biologicals. 2020 Jan;63:97– 100. doi: 10.1016/j.biologicals.2019.11.002 PubMed Web of Science ® Google Scholar
16. European Medicines Agency. Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues; 2014. www.ema.europa.eu/docs/en GB/document library/Scientific guideline/2015/01/WC500180219.pdf
17. Martelli L, Peyrin-Biroulet L. Efficacy, safety and immunogenicity of biosimilars in inflammatory bowel diseases: a systematic review. Curr Med Chem. 2016 Oct 14.
18. U.S. Food and Drug Administration. Information for consumers (biosimilars); 2015. www.fda.gov/Drugs/Development ApprovalProcess/HowDrugsareDevelopedan ddApproved/ ApprovalApplications/TherapeuticBiologicA pplications/ Biosimilars/ucm241718.htm
19. Food and Drug Administration. Biologics Price Competition and Innovation Act. Available at: http://www.fda.gov/ downloads/Drugs/GuidanceComplianceRegu latoryInformation/

HOW TO CITE: Jagruti Pansare*, Shraddha Bhalake, Sayali Erande, Ragini Patil, Biosimilar Drug: Current Situation, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 11, 1674-1679. https://doi.org/10.5281/zenodo.14246072