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Pharmacovigilance In Biosimilars And Biologics

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Abstract

Pharmacovigilance is essential for ensuring the safe use of biologics and biosimilars—medicines made from living systems that are often large and complex in structure. These products can have unique safety concerns such as immune reactions, changes between batches, and risks that may only appear after they are widely used. Monitoring methods like spontaneous reporting, active surveillance, and strong product tracking help detect and manage these issues. Regulatory bodies such as EMA, USFDA, and CDSCO require regular safety reports, risk management plans, and registry-based studies to improve safety tracking. However, challenges remain in tracing batches, interpreting data, and handling product switches. New tools like blockchain for traceability, advanced data analysis, and global safety standards are shaping the next phase of pharmacovigilance. This review discusses the importance of strong monitoring systems to keep biologics and biosimilars safe while supporting their wider use.

Keywords: Pharmacy, Biologics, Biosimilars, EMA.

Introduction

The World Health Organization (WHO) characterizes pharmacovigilance as the scientific discipline encompassing activities focused on identifying, assessing, comprehending, and preventing adverse drug reactions (ADRs) and other pharmaceutical-related complications. Effective pharmacovigilance implementation necessitates the documentation of various categories of presumed reactions to regulatory bodies, including suspected pharmaceutical interactions with other medications or food substances, ADRs linked to drug discontinuation, therapeutic mistakes or excessive dosing, and treatment ineffectiveness.[1]

The traditional ideas of pharmacology and medicine have been overturned by biological drugs. They are now a fundamental component of contemporary medicine and the so-called "personalized therapy" or "targeted therapy," which targets a specific area of the body. In this work, biological medications are referred to as "biologics." Hormones, enzymes, blood products, and immunological medications (serums, vaccines, immunoglobulins, allergens, and monoclonal antibodies) are examples of biologics. [2]

Based on the European Medicines Agency (EMA) characterization of biologics, these pharmaceutical agents comprise one or multiple active components obtained from biological origins. Biologics represent larger and more intricate molecular structures compared to their non-biological counterparts. The reproduction of such complexity is exclusively achievable through living systems.[3]

A biosimilar represents a biological therapeutic product that demonstrates substantial similarity to an originator product manufactured by another company, and may also be termed a follow-on biologic or subsequent entry biologic. [4]

When the patent on the original "innovator" product expires, biosimilars—officially approved versions of the original product—can be produced. [5]An essential part of the approval is mentioning the innovator product. [6]

Table1. Difference between Biosimilars and Biologics

parameter	**Biologics**	**Biosimilars**
Defination	Large, complex molecules developed through biotechnology using living cells.	A highly similar version of an already approved biologic (reference product)
Molecular Complexity	High; exact structure often unknown due to complexity.	Nearly identical but not an exact copy due to inherent variability.
Development Time	10–15 years, involving discovery and full clinical trials.	6–8 years; skips discovery, uses abbreviated approval pathway.
Clinical Trials	Full Phase I–III trials required.	Comparative analytical studies and limited clinical trials (usually Phase I/III).
Approval Process	Standard NDA/BLA with full safety and efficacy data	Abbreviated Biologics License Application (aBLA) with focus on similarity.
Cost	Very high due to long development and R&D.	15–30% cheaper than innovator biologics.
Post-Marketing PV	Mandatory, but generally predictable	More intensive PV needed due to extrapolation of indications and potential batch variability.

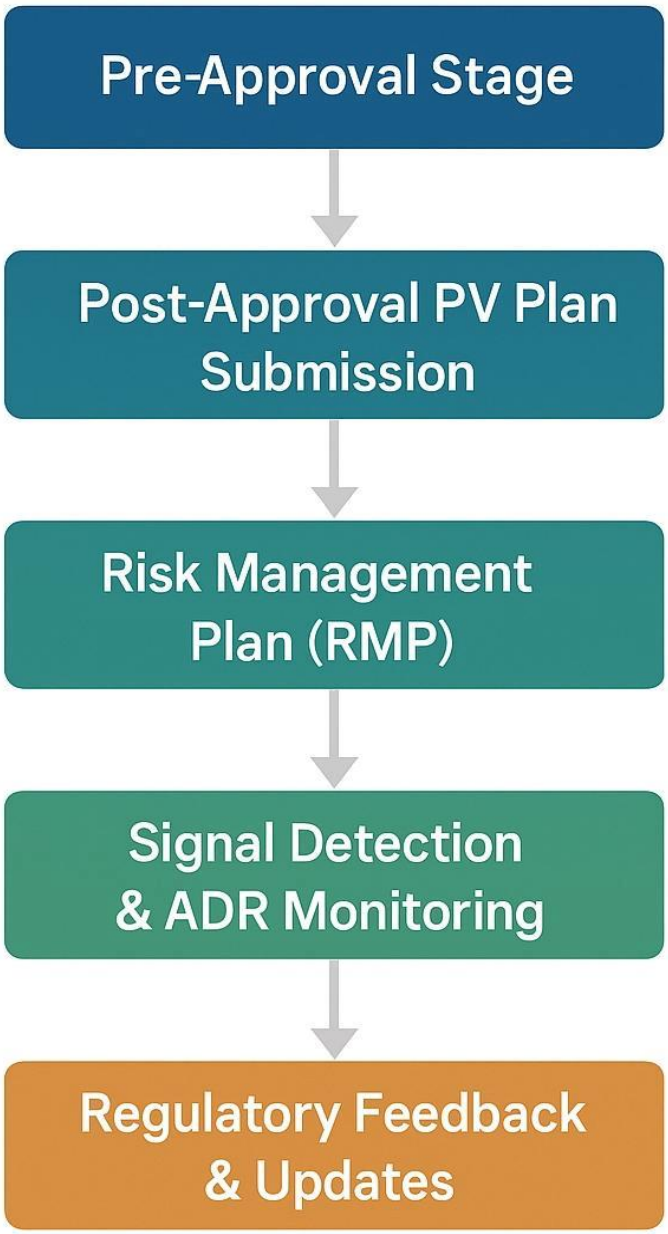

Figure 1. Pharmacovigilance Regulatory Framework for Biosimilars and Biologics

Application of Pharmacovigilance in Biosimilars & Biologics

A. Purpose & Importance of PV in Biologics/Biosimilars

Large, complex molecules made by living systems, biologics and biosimilars are naturally more vulnerable to risks like immunogenic reactions and batch-to-batch variability. Pre-approval studies might not reveal these risks, but widespread use makes them obvious. According to review studies, strong pharmacovigilance systems are therefore required to track long-term safety and identify uncommon adverse events.[7,8,10].

B. Pharmacovigilance Systems: SRS vs Active Surveillance

In post-marketing pharmacovigilance, two primary approaches are employed:

a) Patients and medical personnel can freely report adverse occurrences through spontaneous reporting systems (SRS), which are passive systems. Product misidentification is a major drawback in this context, particularly when biosimilars have similar names [10,12].

b) Active Surveillance (AS): To proactively identify safety signals, this involves database linkage studies or cohort event monitoring. AS offers more precise product-level safety data, which is particularly helpful in hospitals and other care settings [11,13].

C. Traceability Challenges

An essential component of efficient pharmacovigilance is precise product identification. Issues that can impede traceability include comparable container designs, shared INNs among businesses, and a lack of batch-level documentation. As solutions, manufacturer-specific coding and biosimilar-specific naming (such as suffix-based INNs) are suggested [9,10,15]."

D. Regulatory Risk Management Measures

Regulatory innovators, such as the EMA, USFDA, and CDSCO, mandate that periodic safety update reports (PSURs) and a risk management plan (RMP) be submitted at predetermined post-market intervals. These technologies provide mitigation methods and assist in monitoring recognized dangers (e.g., immunogenicity) and new safety issues [7,8,12].

E .Real-World Monitoring via Registries & Databases

In PV, specialized databases and registries across diseases and geographical areas are essential. For example:

-To find safety trends, WHO's VigiBase records worldwide ICSRs [16].

-Europe's EudraVigilance facilitates real-time signal detection and monitoring across the EU [12].

-Disease-specific registries, like BIOBADASER, RABBIT, and ARTIS, monitor the results of biologics and biosimilars in rheumatology, exposing long-term risks and patterns of adverse events in the real world [13].

F. Tailored Recommendations for Emerging Markets

In order to improve biosimilar traceability, the Pharmacovigilance Programme of India (PvPI) recently updated ADR reporting forms in India to better capture specific data points like batch numbers, brand names, and device-related adverse events [14].

Additionally, customized advice highlights:

-Tracking of temperature control during storage or transit,

-Procedures for blood samples for suspected immunogenicity,

-Localized ADR data is used to update prescribing information on a regular basis [14].

Advantages of Pharmacovigilance in Biosimilars & Biologics

- Improved Safety Monitoring Beyond Pre-Approval
  Unanticipated adverse events may surface post-marketing due to abbreviated biosimilar development pathways and structural complexity, making post-marketing pharmacovigilance *"a crucial element to the safe use of biosimilars.[17]
- Enhanced Traceability of Products and Batches
  Clear product identification is supported, with 92.6% of biosimilars in Europe identifiable by specific manufacturer, improving accuracy of ADR reporting. [18]

- Robust Risk Management via RMP Submissions
  Biosimilars require more detailed safety planning than generics, including Risk Management Plans (RMPs) and potential additional risk minimization measures tailored for complex biologics.[19]
- Detection of Immunogenicity and Rare Events
  Pharmacovigilance becomes essential to catch immune responses (e.g., infusion reactions, antibody formation) that were not seen during limited clinical trials. [20]

Disadvantages / Limitations of Pharmacovigilance in Biosimilars & Biologics

- Complexity in Interpretation
  Variability in manufacturing and molecular heterogeneity may cause minor differences in structure or glycosylation patterns, making safety signal detection more difficult. [21]
- Limited Batch-Level Reporting
  Despite good manufacturer-level traceability, batch information is often missing, compromising linkage between ADRs and specific product batches. [22]
- Cost and Operational Demand
  Maintaining robust PV systems—including electronic tracking, RMP updates, and active surveillance—involves higher cost and technical demands compared to generic drugs. [23]
- Challenges in Interchangeability Monitoring
  Switching between reference biologics and biosimilars—or among biosimilars—lacks consistent global regulatory standards, and may risk unknown immunogenic effects or efficacy issues.[24]

Future of Pharmacovigilance in Biosimilars and Biologics

As biosimilars and biologics become increasingly integrated into global healthcare systems, the scope and sophistication of pharmacovigilance (PV) must evolve accordingly. The future of PV in this space will rely heavily on technology, regulatory harmonization, patient-centered systems, and global collaboration to address safety concerns, ensure traceability, and foster confidence in the use of complex biologic products.

1. Integration of Artificial Intelligence and Big Data

Artificial Intelligence (AI) and machine learning (ML) algorithms are expected to revolutionize signal detection by analyzing vast amounts of real-world data (RWD) from electronic health records, social media, and wearable devices. These tools will help in early identification of adverse drug reactions (ADRs), especially rare or long-term events, which are difficult to detect through traditional systems . [25]

2. Advancement in Traceability Through Blockchain and Digital Tools

Improving traceability is vital for effective PV in biosimilars due to the risk of product mix-ups or batch-specific issues. In the future, technologies like blockchain and cloud-based batch tracking systems will ensure secure, real-time traceability, enabling healthcare professionals to identify product-specific safety concerns more accurately [26]

3. Greater Emphasis on Real-World Evidence (RWE) and Registries

Real-world evidence from patient registries will become more critical in understanding the long-term safety and efficacy of biosimilars in various populations. Disease-specific databases like BIOBADASER (rheumatology), RABBIT, and ARTIS will offer valuable longitudinal safety profiles for biosimilars post-marketing .[27]

4. Global Harmonization of Pharmacovigilance Guidelines

There will be a shift toward aligning pharmacovigilance regulations across countries to ensure uniform safety standards for biologics and biosimilars. WHO and ICH are actively working on harmonized guidelines to address naming conventions, labeling, and reporting systems .[28]

5. Adaptive Risk Management Plans (RMPs)

Future risk management will be dynamic, adjusting based on incoming safety data. RMPs will be updated in real-time, possibly through cloud-based platforms, enabling faster response to emerging safety signals .[29]

6. Enhanced PV Infrastructure in Emerging Markets

Countries like India are already revising PV guidelines to better monitor biosimilars, including changes in ADR reporting forms and protocols for immunogenicity testing. These improvements will continue, including better education and digital reporting tools for healthcare providers.[30]

Hierarchy of Risk Management Stratergies in Pharmacovigilance for Biosimilars and Biologics

Figure 2. Hierarchy of Risk Management Stratergies

Conclusion

Biologics and biosimilars have greatly expanded treatment choices but also need close safety follow-up after approval. Pharmacovigilance is key to finding rare or delayed side effects, improving product identification, and following regulatory rules. While existing systems work well in some regions, issues like manufacturing differences, missing batch data, and varying rules between countries still exist. Future improvements may come from AI-based monitoring, blockchain tracking, and better use of real-world patient data. To get the best results from these medicines, a proactive and coordinated approach to pharmacovigilance is needed, combining updated technology, clear regulations, and teamwork between healthcare providers and regulators.

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