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Global Biosimilar Drug Development: Any Chance for Consolidation after 15 Years of Positive Regulatory Experience?

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1. Introduction

Biological drugs are highly innovative pharmaceuticals derived from living cells or organisms for the treatment of high-burden diseases such as cancer, autoimmune/chronic inflammatory, cardiovascular, metabolic and central nervous system diseases. Biosimilar medicines have been developed after the patent expiry of originator biological drugs in order to facilitate access to these effective drugs, at a reduced cost.

2. Discussion

Biosimilar drugs are similar to innovative biological products in terms of their quality, safety and efficacy, i.e. there is no clinically meaningful difference between the originator and the biosimilar product. Biosimilars in the regulated markets are approved according to the same high standards of pharmaceutical quality, safety and efficacy that apply to all biological drugs approved in the EU, US or other countries.

Developers have to demonstrate biosimilarity based on comprehensive comparability studies with the reference medicine. Comparability studies have to be carried out throughout the whole development program, from analytical characterization of the drug substances to pharmacokinetic/pharmacodynamic comparison of the biosimilar and the reference (originator) biological product.

The overall aim of biosimilar development is to demonstrate biosimilarity - high similarity in terms of structure, biological activity and efficacy, safety and immunogenicity profile.

Our understanding of the safety profile of biosimilars is limited due to the nature of the clinical trials carried out during clinical development. This is true, even if regulatory agencies require extensive demonstration of similarity e.g. immuno-

genecity testing, assessment of adverse events etc. in a clinical trial setting. This substantiates the need for collecting post-marketing safety data, to judge potential safety concerns in clinical practice. The overall safety of using biosimilar drugs is substantiated by the more 700 patient days accumulated so far.

The European Medicines Agency developed pioneering scientific principles and a tailored regulatory framework for the review and regulatory approval of biosimilar products. This core concept has been successfully implemented not only in the European Union, but many local authorities, such as Biologics and Genetic Therapies Directorate (Canada), PMDA (Japan), TGA (Australia), KFDA (Korea) have applied a very similar approach.

Since the approval of the first biosimilar product in the European Union in 2006, biosimilar approvals intensified in the recent years, reaching over 50 successful registrations in the EU. The EU/EMA has completed the most registrations of biosimilar medicines so far, significantly exceeding approvals by US FDA. By the end of 2018, only 15 biosimilars to 9 reference products have been approved by US FDA

The positive evidence acquired over 15 years of clinical experience with biosimilar drugs in the EU demonstrate, that these drugs can be used absolutely safely and effectively in all approved indications.

Biosimilar medicines have successfully contributed to lowering the cost of biological therapies. According to analysts, the global biosimilar market could reach 78 billion EUR by 2020. Certain countries established advanced local regulations to intensify biosimilar uptake, e.g. France has established the framework for automatic substitution of certain biosimilar products at the pharmacy level for naïve patients. However, even the position of EU regulatory agencies are heterogene-

ous in terms of interchangeability, with several countries averting automatic substitution yet.

4. Conclusions

The success of the biosimilar concept is substantiated by the positive experience with biosimilar drugs especially in the European Union. Major national authorities have been implementing (global) standards for development and regulatory approvals, mostly relying on the EMA guidelines and the WHO's regulatory framework. WHO's global standards regarding the quality, efficacy and safety of biosimilar products can be a

suitable basis for mutual recognition and convergence of regulatory oversight at the global level.

References

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