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Present And Future Status Of Biosimilars In India

Rakesh R. Somani Professor and Principal, School of Pharmacy, DY Patil Deemed to be University, Navi Mumbai. rakesh.somani@dypatil.edu

Abstract:
Biosimilars or similar biologics are pharmaceutical products mimicking the already marketed biological medical product. It is just like the innovator product. Biologics or biopharmaceutical is any pharmaceutical drug product synthesized, extracted from, or semi-synthesized from biological sources. They could be vaccines, blood, blood components, allergenic, somatic cells, gene cures, tissues, recombinant therapeutic protein, and living cells used in cell remedies. Biologics may be sugars, proteins, nucleic acids, or a complicated combination of those materials, or can be live cells or tissues. They (or their precursors or components) are obtained from living sources—human, animal, plant, fungal, or microbial. Various terminologies are used to define Biosimilars by different regulatory bodies. Such names terminologies include Follow-on Biologics (US-FDA, Brazil), Similar Biotherapeutic Product (WHO), Similar Biologics (India), Biosimilar (Europe), and Subsequent entry Biologics (Canada).

Keywords: Biosimilars, healthcare, Biotherapeutic, WHO.

Introduction

Biosimilars are products that are manufactured whilst the patent of the innovator biological product expires. Subsequently, they are a generic version of a biological drug. Small generic drug molecules can be easily copied after the patent expiry in terms of overall chemical synthesis, production approaches, pharmacokinetic and pharmacodynamic parameters, biological activity, etc. but, biologicals are massive and particularly complex molecules that cannot be easily mimicked in production and procurement procedures. Hence it is very important to mimic the pharmacokinetic parameters of the innovator product for regulatory approval. Regulatory bodies all over the globe have initiated norms for advertising and marketing biosimilars to ensure quality, protection, and efficacy. Biosimilars are evolved and evaluated by the use of rigorous approaches, concerning unique analytical and functional studies, non-clinical assessments, and clinical trials.

Developing biosimilars requires a high degree of technical knowledge due to the complicated structure of these molecules. The clinical trials done on a potential biosimilar are designed in a different way to the ones for approval of a novel biologic. Assessing biosimilar, the aim is to verify that there are not any clinically significant variations in its efficacy and safety compared to the reference product. Biosimilar approval is based on the totality of facts demonstrating the similarity between the

biosimilar and the reference product, such as quality traits, biological activity, safety, and efficacy. Because of this, it is very difficult to develop a biosimilar product as compared to the development of a generic drug.

Regulatory guidelines India v/s World: EMA (European Medicines Agency) first developed regulatory guidelines for the approval of biosimilars from 2005 to 2006 and since then it has developed many general and specific guidelines. Omnitrope (somatropin) was the first product approved in the EU as a biosimilar in 2006. The Biologics Price Competition and Innovation Act of 2009 (BPCIA) allows the licensing of biosimilars for previously licensed reference products in the USA. India drafted itsfirst regulatory guidelines for 'similar biologics' in June 2012 and finalized guidelines were implemented in September 2012. The proposed rules define specific requirements for pre-marketing and post-marketing data, apart from preclinical studies and clinical data.These efforts are aimed at upgrading and maintaining the quality of biosimilar products that are manufactured in India. In the development of these guidelines, the department of biotechnology and the drug regulator (CDSCO) has given references of ICH guidelines so that products developed and imported in India will be according to the global regulatory standards so that Indian manufacturers can establish a technological advantage in ensuring the safety, quality, and efficacy of the products.

Market Scenario: During the past few years more than 50 biopharmaceutical products have been approved for marketing in India with more than half of them being biosimilars. Recognizing this opportunity, India has taken steps to make a mark in the biosimilar sector. Many major drugmakers have already outlined plans, identified products, and set aside budgets for developing new products. Major Player like Dr. Reddy's laboratories has already launched a few of its important biosimilars. Also, Cipla has started making huge investments in India and outside to acquire manufacturing facilities and product pipelines in the biosimilar segments. The company has acquired facilities in India and China to develop biosimilars. Similarly, companies like Wockhardt and Lupin have initiated their efforts in the said field.

Patent worth around $ 80 billion of biosimilars was expected to expire globally by the end of 2015. The global biosimilar market has expected to reach $ 6.22 Billion by 2020 from $ 2.29 Billion in 2015. India shares 75% of the biosimilar market, in which 30 biosimilar products are marketed out of 40 biological products. The Indian biosimilar market is being prepared for big growth, stimulated by the launch of new biosimilars, growing popularity, and the entry of new players such as Aurobindo Pharma. It is expected to increase from $186 million in 2016 to $1.1 billion in 2020, according to industry estimates. India's biopharmaceutical company Biocon, which ranks among the top three biosimilar global players for insulin, has had multiple successes in its container since its inception. So far, Biocon has successfully taken seven biologics, novels, and biosimilars from laboratory to market in India.

Comparing Indian Biological prices to the rest of the world

Substance	Average world price	Average Indian price	Differential in %
Human Insulin	U$ / 100 IU vial	US$6.50 / 100 IU vial	80%
Anti-EFGR Monoclonal	$25,000 per treatment	$6,000 per treatment	75%
Recombinant streptokinase	$150 / vial	$10 / vial	95%
EPO	$200 / 2,000 IU	$10 / 2,000 IU	95%

Source: Biocon (Biosimilars India 2009)

Biosimilars have the capability to deliver a number of benefits to the healthcare benefits to the healthcare community. The main advantage is the reduction in cost which is done by almost 20-25 % of the original innovator product. This may be due to a reduced number of clinical trials and research and development which goes into the discovery of novel biologics. Also, they help in expanding the available options for treatment and thus positively impact patients' life by treatment of life-threatening diseases or chronic diseases, such as cancer and rheumatoid diseases. The introduction of biosimilars has induced a new kind of innovation ideology for the pharmaceutical field. Realization of audience needs and catering to them is the ultimate motivation for the fulfilment of absolute potential and healthcare benefits to the healthcare providers and patients together. It has now become crucially important to proactively seek innovations due to the rise in detrimental diseases all around the globe. Initiating new platforms and partnerships is the need of the hour to improve health conditions.

Challenges for India: Biosimilar makers have to face more difficulties in the development, clinical assessment, manufacturing, registration, and product marketing as compared to generics. Development of biosimilar is not very easy due to the high expense, the difference in the development process, the need for sophisticated instruments, and the training process. The future relies upon satisfactory execution of the pharma covigilance framework and administrative rule while India's pharma covigilance framework is still under betterment. Indian manufacturers bearing this cost without increasing the price of the product is a big challenge. The development of biosimilars needs research and development facilities to make an identical copy of the original innovator product or generic product. A comparison function must be carried out with the innovator product at all levels of product development, which includes:

physicochemical attributes, bioactivity, preclinical in vivo comparison, Phase I PK and safety, and Phase III efficacy and safety. This can be tough due to the fact that information for the innovator product might be lacking. The only way to obtain information is based on the innovator product which is available in the market. The different sources of variation between the biosimilar product and innovators' product can be as follows:

• Use of different vector
• Different cell expression system
• Different cell line growth media and methods of expansion
• Different operating conditions
• Different binding and elution conditions
• Different methods, reagents, reference standards

Visiongain, one of the fastest-growing business intelligence providers based in London, in its recently published report analyzed 25 leading developers, producers, and marketers of biosimilars worldwide. Its report discusses biosimilar competition for these five therapeutic agents:

- Adalimumab
- Infliximab
- Etanercept
- Darbepoetin alpha
- Rituximab

The leading biosimilar companies in India, according to the survey, are:

- Biocon
- Dr. Reddy's Laboratories
- Wockhardt
- ZydusCadila
- Ranbaxy
- Reliance Life Sciences
- Intas Biopharmaceuticals.

Optimistic Future for India: Indian pharmaceuticals market is the third-largest in terms of volume and thirteenth largest in terms of value, and it accounts for 20 percent in the volume terms and 1.4 percent in value terms of the Global Pharmaceutical Industry as per a report by Equity Master. India is the largest producer of generic drugs globally with the Indian generics accounting for 20 percent of global exports in terms of volume. The Indian government has taken many steps to reduce costs and bring down healthcare expenses. The ease of regulatory approval for generic drugs has been increased to facilitate low-cost and high efficacy drug. Speedy introduction of generic drugs into the market has remained in focus and is expected to benefit the Indian pharmaceutical companies. India's cost of production is nearly 33 percent lower than that of the US. Labor costs are 50–55 percent cheaper than in Western countries. The cost of setting up a production plant in India is 40 percent lower than in Western

countries. India has a skilled workforce as well as high managerial & technical competence in comparison to its peers in Asia. Keeping all this in view, we can certainly hope that in the near future, India can emerge as the global leader in biosimilars, the future of biological therapy. Large opportunities remain for biosimilars, with the study predicting high, rapid market expansion from 2016 to 2026.

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