INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

ISSN:2320-2831

IJPAR |Vol.9 | Issue 2 | Apr - Jun - 2020

Journal Home page: www.ijpar.com

Review article ***Open Access***

Biosimilars – an overview

Vijaya Boga*, R. Prasanthi

Assistant Professor, Sarojini Naidu Vanita Pharmacy Mahavidyalaya

***Corresponding Author: Vijaya Boga**

ABSTRACT

Biosimilars are a new class of drugs intended to offer comparable safety and efficacy to the reference. Biologic products are being developed over the past three decades. The expiry of patent protection for many biological medicines has led to the development of biosimilars in UK. Biosimilar or similar biologic use has increased in the recent years following the approval of the first biosimilar in early 2000. India is one of the leading manufacturers of similar biologics. India has developed a new guideline in 2012 for the pre- and post-marketing approval of similar biologics. The overall risk is modest with Biosimilars, but regulatory pathways are required because of structural complexity, manufacturing process and risk for immunogenicity. In the last few years, India has seen a robust development in its biosimilar portfolio. The Indian biosimilar market is composed for big growth, by the launch of new products and growing acceptance of biosimilar. India's top manufacturers are also entering the biosimilars market, with more than 50 biosimilar products approved by the Central Drugs Standard Control Organization (CDSCO). This review shows the evolution of biosimilar development regarding regulatory, manufacturing bioprocess, comparability, and marketing.

Keywords: Biosimilars, Biological products, Biotechnology, Reference product

INTRODUCTION

Biological products

Biological products are generally large, complex molecules produced through biotechnology (i.e., recombinant DNA technology, controlled gene expression, or antibody technologies) in a living system, such as a microorganism, plant cell, or animal cell. After production of complex biopharmaceuticals, an innovator puts to get approval from regulatory authority, with brand name and is protected under patent rights. The chemical structure of the product is not disclosed to others. Simultaneously or after some period another manufacturer may discover complex molecule using a different source of cloning or process with a structure known or not known but the product may show the same biological effect as a product of the first innovator and this second product is considered as a generic version.

Reference product

A reference product is the single biological product, already approved by FDA, against which a proposed biosimilar product is compared. A Reference Biologic is utilized as the comparator for comparability studies with the Similar Biologic in command to show Similarity in terms of safety,

efficacy and quality. In India, a reference biologic is one which has been granted a marketing authorization in India by DCGI on the basis of a complete dossier and with a history of safe use in India.

Biosimilar

A biosimilar can be defined as a biological medical product highly similar to another already approved biological medicine. Indian guidelines define a "Biosimilar" as a biological product or drug produced by genetic engineering techniques and claimed to be "similar" in terms of safety, efficacy and quality to a reference biologics, which has been authorized by Drug Controller General of India (DCGI) for safe use in India. The pharmaceutical form, doses and route of administration of the biosimilar and the reference product should be the same. In approving biosimilars, the FDA may require that manufacturers conduct a clinical study (or studies) sufficient to establish safety, purity or potency in one or more uses for which the reference product is licensed. If the reference product has more than one indication, the safety and efficacy for all indications have to be justified or demonstrated for each indication separately.

Different regulatory bodies use different terminologies for biosimilars - in Europe "similar", the United States, Brazil and Japan- "follow on biologics", Canada- "subsequent entry biologics" Mexico – "biocomparables", India – "similar biologics" WHO – "similar biotherapeutic product".

WHO Definition

"A bio therapeutic product that is similar in terms of quality, safety and efficacy to an already licensed reference bio therapeutic product"

USFDA Definition

"A biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product"

Characteristics of Biosimilar

- High molecular complexity
- very delicate to changes in manufacturing processes
- Variances in impurities and/or breakdown products can have serious health implications.

Advantages of Biosimilars

- There is huge market needs and growing affordability for Biosimilars in universal and domestic market.
- Development and manufacturing of Biosimilars are improved by existing manufacturing technology
- Due to no investment in phase I-II of clinical trials, Biosimilars are existing at cheaper prices than the reference products, so treatment price with Biosimilars is minor than innovators biological drug.
- Biologic medicines can be really expensive. Having multiple biosimilars in the market will break the reference drug monopoly and help bring down the costs
- With more biosimilars in circulation, more patients worldwide can have access to these treatment options

Disadvantages of Biosimilars

- Biosimilars are not as much of stable as chemical based pharmaceuticals and thus essential cold chain distribution and have a shorter shelf life. This increases the price and complexity of distribution.
- The cost of development will be importantly higher than for chemical based generics.
- The required capital venture in property plant and equipment and the cost of manufacturing will be much greater for Biosimilars than for generic drugs

Challenges of Biosimilars

- Patient and prescriber education: It is difficult for reviewing clinical data, discussing substitution with pharmacists, and so forth. The physicians, pharmacist and patients, all need to be enlightened and subsequently, convinced of the benefits of switching to biosimilars.
- Extrapolation issue: It is a question for the prescriber whether the biosimilars can be prescribed for off-label indications that are accepted for the reference drug.
- The interchangeability question: substitution of a reference drug with biosimilar or vice versa is another avenue seeking reconciliation.
- Rare diseases: Rare disease treatments often utilize "orphan drugs" that are associated with high costs. Developing biosimilars for these

orphan drugs may face many practical problems. First, it is difficult to obtain a large, non-heterogeneous population for phase I and III trials. Furthermore, the cost of manufacturing enough batches of the biosimilar to run batch-to-batch variability studies can be disproportionately high.

Difference between Biosimilars and generics

Biosimilars differ from generic drugs because their active ingredients are huge complex molecules. Such molecules are nearly impossible to reproduce in every aspect. Even minute variations in production yield slight differences. Unlike to chemical molecule, making a biosimilar in all aspects are very difficult. Generic products are similar in chemical structure as well as in the manufacturing process as that of original product but biosimilars are having a similarity only in therapeutic applications.

Some of the biosimilar products approved in India

India has approved a Biosimilar for hepatitis B in 2000, but during that time there was no specific guideline for development and marketing of Biosimilars in India. Later many Biosimilars were developed and marketed in India by various Pharmaceutical companies. Though India was one of the first countries in the world to use it, there was no specific guideline available for "similar biologics," and approval process for Biosimilars is more cumbersome and require more data than other generic drugs. Hence to address the challenges associated with the development of Biosimilars, Central Drugs Standard Control Organization (CDSCO) in collaboration with the Department of Biotechnology (DBT) has developed "Guidelines on Similar Biologics; Regulatory Requirements for Marketing Authorization in India" in 2012 and has revised it in 2016. Cipla launched India's first biosimilar of Etanercept (Etacept) in April 2013, Intas launched India's first biosimilar of Rituxumab (Mabtas) in April 2013 & Ranbaxy launched India's first biosimilar of Infliximab (Inflimab) in December 2014. The following are few top biosimilars in India.

Company	Product name	Active drug	Indication
Intas	Intacept	Etanercept	Rheumatoid arthritis, psoriatic arthritis
Emcure	Epofer	Epoetin alfa	Anaemia
DRL	Grafeel	Filgrastim	Neutropenia
Zydus cadila	Exemptia	Adalimumab	Ankylosing spondylitis
Gentech (Roche)	Herceptin	Trastuzumab	Breast cancer
Biocon	Insugen	Human Insulin	Diabetes mellitus

Manufacturing of biosimilars

Manufacturing a biologic consists of genetically modifying a cell, which becomes the basis for a cell line used for the production of the necessary protein for the biologic medicine. The protein is then separated from the cells and purified. Biosimilars are created from small alterations to the manufacturing process which creates a molecule that is not identical but closely resembles the reference product. While the differences in the biosimilar molecule might be slight, these changes in the manufacturing process of a biosimilar can affect the efficacy and safety of a biosimilar compared to the reference biologic.

Current status of Biosimilar in Indian Market

Indian Pharmaceutical industry has grown as global market leader in Biosimilars because of its thriving Biosimilar ecosystem than other countries. In the last few years, India has seen a robust development in its biosimilar portfolio. The Indian biosimilar market has growing acceptance of biosimilars. Biotechnology product in India was around US$ 200 million in the year 2008; it reached to US$580million by 2012 and expected to worth more than US$ 167 billion by 2015-2016. The achievement of this target may be positioned the Indian biosimilar producer as top five of the top ten

position (ICIS report). According to ASSOCHAM-Sathguru report released in 2016, Indian biosimilar industry presents a US$240 billion global market opportunity and a domestic market is expected to grow US$40 billion by 2030.

Future prospects for Indian Manufacturer

Development of biosimilar is not very easy due to the high expense, the difference in the development process, need a sophisticated instrument and training process. How Indian company bears this cost without enhancing the price of the product is a big challenge. Development of biosimilars needs Research and Development facilities which make an identical copy of original innovator product or generic product. The market competition driven by biosimilars can pose threat to the monopoly of the brand pharmaceutical industry. In the coming years, the regulatory authorities need to provide a more tangible framework to address some grey areas in the marketing and prescription of biosimilars.

CONCLUSION

Since the use of the first biosimilar, the development and uses of "biosimilars" have witnessed substantial growth. Every year, regulatory agencies are granting approval of various similar biologics for the treatment of many cancerous and noncancerous diseases. India has firmly established itself as a global player as a maker of biosimilars. It is also a huge market for the biosimilars because of its rapidly increasing population. Although the potential is high and expectation is huge for India, the challenges are also enormous and formidable to maintain the leadership. Biosimilar maker needs to face unusual problems in the development, clinical improvement, manufacturing, registration and product marketing contrasted with customary generics. To achieve the true potential and continue as a global leader, Indian biopharmaceutical companies need to upgrade their technology and have to improve the manpower skill. For this, they need an enabling environment from the government and regulatory agencies.

REFERENCES

[1]. Khomendra kumar sarwa and vijayendra kumar suryawanshi, Biosimilars in India: challenges on acceptance and future prospect, PhTechMed, 5(1), 2016.
[2]. Pooja paul, Harvinder popoli, Ankit saxena, Anamika Jaiswal and sudha sah, "Current scenario of biosimilar", The pharma innovation journal 7(7), 2018, 188-193
[3]. Jay P Desai: Bridges to the Bloom: The Future of Indian Biosimilars, Biosimilars_ RAJ Pharma 2009.
[4]. Sekhon BS, Saluja V: Biosimilars: an overview, Expert Opinion Biosimilars 1, 2011, 1–11.
[5]. Global Biopharmaceutical Market Report (2010– 2015) IMARC 234, 2010.
[6]. Anitha nandagopal, Yusra shakeel and Mamata tirunagiri, "Biosimilars: Current Scenario and Challenges in India", Acta Pharm. Sci. 56(1), 2018.
[7]. Roger SD, Goldsmith D. Biosimilars: it‟s not as simple as cost alone. J Clin Pharm Ther. 33, 2008, 459–464.
[8]. Current Scenario of Biosimilar. http://www.dbtindia.nic.in/wp-content/uploads/10.- Guidelines-on-Similar-Biologics-2016.pdf
[9]. Nandini T, Rajagopalan R. An Overview of Similar Biologics. 2, 2013, 833-842.
[10]. Bikash R. Meher, Sakthi Balan, Smita Das et.al, Biosimilars in India; Current Status and Future Perspectives, J pharm & bioallied sci. 11(1), 2019, 12-15.
[11]. Current Scenario of Biosimilar. https://www.persistencemarketresearch.com/marketresearch/biosimilars-market.asp
[12]. Current Scenario of Biosimilar. https://www.mordorintelligence.com/industryreports/global-biosimilars-market-industry