Chapter 7
Biosimilars: Concept and Regulation

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ABSTRACT

Biosimilars are a new class of drugs, which are derived from live organism through the recombinant DNA technology. These are recently introduced in the pharmaceutical field for the preparation of drug to prevent or control the diseases. Patients with diabetes and renal failure may already be receiving biosimilar epoetin and may receive same insulin in coming years. The main aim of present article is to introduce the fundamentals of biologics and to explain how they are different and what these differences mean for pharmacists.

INTRODUCTION

Biosimilars also called follow-on biologics are biological medical products, whose active moieties are generated from a living organism via recombinant DNA or controlled gene expression methods. These terms are used to portray officially approved ensuing types of innovator biopharmaceutical products designed by a different sponsors following patent and exclusivity expiry of the innovator's product (Nick, 2012). The definition of biosimilars by different regulatory authorities is as follows:

1. **The World Health Organization:** A biotherapeutic product, which is similar in terms of quality, safety and efficacy to an already licensed reference biotherapeutic product (WHO, 2009).
2. **The European Medicines Agency:** A biological medicine that is generated to be comparable to an existing biological medicine (the 'reference medicine'). Upon approval, a biosimilar's variance

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and any deviation between it and its reference medicine will have to be shown not to affect safety or effectiveness (EMA, 2012).

3. **The U.S. Food and Drug Administration:** A biological product that is remarkably comparable to a U.S. licensed reference biological product notwithstanding minor differences in clinically inactive components and for which there are no clinically meaningful divergence between the biological product and the reference product in specifications of the safety, purity and potency of the product (USFDA, 2012).

The use of biotechnology to develop medicines is rapidly growing and it is estimated that biological medicines are likely to become the biggest selling medicinal products by 2016 (Pharmacophorum, 2012). Global Industry Analysts Inc. (GIA) has forecasted that biosimilars market around the world is expected to achieve $18 billion by 2017 (GIAI, 2012). Driven by the passing by the US Congress of the 2010 Biologics Price Competition and Innovation Act (BPCI), it is also suggested that the US will go beyond Europe during analysis period to become globally largest market for biosimilars in the near future.

Biotechnology uses proteins, enzymes, antibodies and other substances that are produced in the human body to create biological medicines. Living organisms are also used in the production of these medicines, including plant and animal cells, bacteria and viruses. Biological medicines are much more complex than conventional medicines, which are comparatively simpler chemical molecules (APG, 2011). Since 2006, 13 biosimilars have been granted marketing authorizations in the EU (EBE-EFPIA, 2006) and the use of these presents challenges for clinical practice that are different to those that relate to conventional generic medicines.

All biotechnology products, including biosimilars have different starting materials and manufacturing processes, which means they have different characteristics that may not be detectable in conventional clinical trials such as rare adverse drug reactions, especially events that are immune mediated. This key difference has influenced the current legislative framework for biosimilars, which treats biosimilars differently to conventional generic medicines (EBE-EFPIA 2006). Biosimilars present a different set of challenges as compared with conventional generics. Further market approval for biosimilars is much complicated. The intricacy of biopharmaceuticals renders it hard to circumvent heterogeneity among batches from the same manufacturer and between the same products from different manufacturers (Crommelin et al., 2005). Moreover, it is not easy to ascertain therapeutic equivalence of biosimilars with reference products and compounds used in clinical trials (Roger, 2006; Chirino and Mire-sluis, 2004; Locatelli, 2006).

Need of Biosimilars

Medicinal products generated by biotechnology make an essential part of medicaments available to patients nowadays. They represent about 6% of the pharmaceuticals presently marketed and account for more than 9% of gross pharmaceutical expenses (IMS Health, 2009). More significantly, one third of products in the pipeline are derived biotechnologically. A number of main biotechnology derived medicines are, or will soon go off patent (Mellstedt et al., 2007). This brings up competition to the market, which facilitates patient reach to safe, effective and more affordable biotechnology-derived products. The prices of the innovator products would remain artificially high in absence of competition. At the same time, fair competition will serve to trigger research for new medicines.