Concept of biosimilar products in Jordan

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Abstract

After the expiration of patents on originator biological products, Jordanian local manufacturers and the agents of international pharmaceutical companies in Jordan started to submit registration dossiers for biosimilar products. The Jordan Food and Drug Administration (JFDA) is the national regulatory authority responsible for the registration of biosimilar products. Biosimilars are registered under the same regulations used for drugs until specific guidelines for registration of biological and biosimilar products are released. Those regulations are called Criteria of Registration of Drugs, Vaccines, Sera and Biological Products, the Renewal of its Registration and the Cancellation of Any of them which was published in the official gazette in 2004 under the Provisional Law Number 80 of the year 2001, Drug and Pharmacy Law and its amendments of the year 2003. Also, the JFDA follows the EMA guidelines on similar biological medicinal products for specific active biological substances for non-clinical and clinical studies requirements and the EMA guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: quality issues. A post marketing surveillance study is requested after a biosimilar product is authorized.

The JFDA keeps pace with all advances in the regulatory issues related to biosimilars in order to be capable of authorizing biosimilar products with a safe, effective and good quality profile.

1. Introduction

The prevalence of type 2 diabetes mellitus and impaired glucose tolerance is increasing in Jordan [1] making insulin one of the most important biotherapeutic products in the Jordanian market as is the case worldwide. Anti-cancer biological products are considered another group of important biotherapeutic products since cancer is the second most frequent cause of death after heart disease in Jordan [2]. A total of (4606) new cases of cancer among Jordanians were registered in 2005 [4]. These data show the increased burden on the government and patients regarding healthcare expenditure taking into account the high cost of originator biological products.

After the expiration of patents on originator biological products, and taking into consideration that in 2013–2015 it is estimated that several biological products representing US $20 billion in annual sales are anticipated to lose patent protection [5], Jordanian local manufacturers and agents of international pharmaceutical companies started to submit registration dossiers for biosimilar products so as to provide the local pharmaceutical market with biological products with competitive prices compared to the expensive reference biological products (RBP). However, there is a concern that, because biosimilars may not be considered interchangeable nor substitutable with their reference/originator products and due to the high cost of developing biosimilars, cost savings to patients using biosimilars will be minimal [6].

Jordan has been a member in the World Trade Organization (WTO) since 2000 and the Jordanian Law of Unfair Competition and Trade Secrets No. 15 of 2000 was issued consistent with WTO agreement on Trade-Related aspects of Intellectual Property Rights (TRIPS). According to this law, data protection for new chemical entities lasts 5 years [7] provided that the registration dossier of the product to be protected is submitted to Jordanian regulatory authority within 18 months of its first date of registration internationally [8] and the same applies to biological products.

Until now there is no local manufacturer that started developing its own biosimilar product. Only one local manufacturer is working on a biosimilar product where the bulk material was bought from a foreign manufacturer and will be formulated into the final product in Jordan. Other manufacturers are contract manufacturing...
with foreign manufacturers where only the secondary packaging and batch release step will be done in Jordan.

2. Products information: current situation

Only one product was authorized as a biosimilar in 2009. Ten biosimilar products have been filed in 2008, 2009 and 2010, nine of which are under review. On the other hand, one product which was submitted in 2005 has failed our approval process in 2009 due to incomplete clinical and quality data.

3. Legislative basis and approach

The Jordan Food and Drug Administration (JFDA) was established in 2003 as the sole national competent authority for drug safety and efficacy and food safety and quality. It is divided into two main directorates, the Drug Directorate and Food Directorate, in addition to other supporting directorates. The Registration Department, which is part of the drug directorate, is responsible for registering drugs according to approved guidelines set by the Prime Minister and published in the official gazette.

There are several working committees in the drug directorate which are formulated according to the Provisional Law Number 80 of the year 2001, Drug and Pharmacy Law and its amendments of the year 2003. The Technical Committee for the Registration of New Drugs is the committee responsible for registration of originator, new drugs and biological and biosimilar products. The chairman of this committee is the secretary general of the Minister of Health and the vice chairman is the director of the drug directorate. Its main responsibilities are to authorize new drugs and study any updates regarding drugs safety and uses and to make decisions concerning different safety, efficacy and quality issues.

At present, biosimilar products are registered under the same regulations used for drugs. Those regulations are called Criteria of Registration of Drugs, Vaccines, Sera and Biological Products, the Renewal of its Registration and the Cancellation of Any of them which was published in the official gazette in 2004 under the Provisional Law Number 80 of the year 2001, Drug and Pharmacy Law and its amendments of the year 2003. However, the registration of Biological and Biosimilar Products differs from the registration of conventional drugs in the following ways:

- The manufacturing site/sites of the active ingredient(s) and intermediate product/s must be accredited.
- For biosimilars, comparative non-clinical, clinical and quality requirements must be met (according to EMA guidelines).
- Batch record of three consecutive batches of the finished product must be submitted.

It should be noted that Jordan is presently implementing the Common Technical Document (CTD).

According to article 9-a of the Criteria of Registration of Drugs, Vaccines, Sera and Biological Products, the Renewal of its Registration and the Cancellation of Any of them: "The Committee decides on any application for registering new drugs and the drugs that have a registered equivalent. It does this within a maximum period of one hundred and eighty days (180) from the date of the submission of the application of completed documents to the Directorate", provided that the applicant submitted all requested data. In addition, according to article 9-b: "The Committee decides on any application of completed documents for registration of equivalent drugs the information of which is protected or which is protected by a Patent Right within a maximum period of 180 days before the expiry of the protection, provided that the resolution for registration is issued on the next day of the expiry of protection".

Prior to 2006, a few non—innovator products were registered as generic medicines. In 2008 the JFDA started to review them as biosimilars. For registration as biosimilars, dossiers are reviewed and evaluated by referring to the EMA guidelines on similar biological medicinal products for specific active biological substances (e.g. recombinant human soluble insulin) as our reference for non—clinical and clinical studies requirements for demonstration of similarity in terms of safety and efficacy between the reference biological product (RBP) and the biosimilar product. Also, we follow the EMA guideline on similar biological medicinal products containing biotechnology—derived proteins as active substance: quality issues, in order to be able to demonstrate that the biosimilar product has a quality profile similar to the reference product.

In order to monitor the safety and to ensure continuous benefit—risk evaluation of the authorized biosimilar product, a post marketing surveillance study is requested after its release in the Jordanian market. This is considered to be mandatory especially since until now no clinical studies were done in Jordan because by contract manufacturers. Local manufacturers depended on the same clinical trials conducted by the contractor. The choice of reference biological product is based on the international registration date of a particular product (the first product registered internationally with a particular active ingredient). Once a biosimilar product is authorized, it is not considered as a RBP. There is still debate regarding interchangeability and substitutability of the biosimilar product with the RBP as is the case worldwide [6].

4. Jordanian guidelines and WHO guidelines/plan to implement WHO guidelines

We are working on draft guidance for registration of biological and biosimilar products. Our references are EMA guidance, ICH guidelines and WHO guidelines. The experience we are gaining from evaluating the registration dossiers of biosimilars submitted to the JFDA and lessons learnt from our practice are considered a good background for developing our own guidelines. It is expected that the Jordanian biosimilars guidelines will differ from WHO guidelines with respect to issues specific to Jordanian regulations since WHO guidelines offer a basis for countries on which each country can develop its own guidelines. For example there is a difference in the choice of the RBP where in Jordan we consider the RBP, as mentioned above, as the first product registered internationally with a particular active ingredient, while WHO gives a general definition only. Also we refer to the EMA guidelines for non—clinical and clinical studies requirements for specific active biological substances.

5. Conclusion

In conclusion, the Jordan Food and Drug Administration, as a regulatory authority shares the same concerns and challenges of other regulatory authorities in the biosimilar products registration field, and will keep pace with all updates and advances in the regulatory issues related to biosimilars in order to be capable of authorizing biosimilar products with a safe, effective and good quality profile.

Conflict of interest

Author has disclosed no potential conflicts of interests.
References


