Towards regulation of similar biotherapeutic products: Thailand’s perspective

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Abstract

The implementation of universal health coverage scheme in Thailand allows quality, equitable and accessible health care for all. Patients with life threatening and chronic diseases can get access to biotherapeutic products to treat their ailments. This triggered a major impact on the need for specific guidelines in evaluation of similar biotherapeutic products in order to standardize the regulatory pathway to license this class of products ensuring that the products meet acceptable levels of quality, safety and efficacy. The development of similar biotherapeutic products (SBP) should be considered to ensure therapeutic equivalence of biotherapeutics products at more affordable prices. This will lead to greater ease and speed of approval and assurance of the quality, safety and efficacy of these products. Therefore, we report herein the SBP situation in Thailand.

1. Introduction

Thailand is one of many developing countries with a universal health coverage scheme whereby many biotherapeutic products have been recognized and tender public purchased by the National Health Security Office in order to treat life threatening and chronic diseases e.g. EPO, interferon and monoclonal antibody. The innovator and original biotherapeutic products are very costly thereby limiting their access to patients, leading to the acceptability of those biotherapeutic products, which have been subsequently licensed to original products by Thai Food and Drug Administration (TFDA) because of their affordable prices.

2. Legislative basis for biotherapeutic products

By definition biotherapeutic products are classified as drugs and have been regulated under legal framework of Drug Act B.E 2510 (A.D. 1967) therefore the same regulations pertaining to drugs shall apply. However there is some minor difference with respect to clinical data requirements. For biotherapeutics, clinical efficacy should be proved whereas bioequivalence is required for generic drugs.

According to the provision of the Drug Act, no renewal of marketing authorization is required as its validity is warranted throughout the entire lifetime of the authorized licensee. Nevertheless, the marketing authorization shall be automatically withdrawn if neither importation nor production of two consecutive years is met.

3. Approach for similar biotherapeutic products

With advancement in biotechnological sciences, there has been a rapid expansion in developing and manufacturing of biotherapeutic products. This is especially true with respect to similar biological products.

At present TFDA has no specific guidelines in evaluating similar biotherapeutic products by which there is a need to justify the therapeutic equivalence between the innovatives with biosimilar products.

Therefore, TFDA has established a technical subcommittee called “Subcommittee on Biosimilar Products” to review current situations and existing regulations in order to develop such guidelines based on WHO’s guideline on evaluation of similar biotherapeutic products (SBP). The objective is to strengthen the evaluation and assurance of quality, safety and efficacy of similar biotherapeutic products thus increasing the credibility of therapeutic equivalence of biotherapeutic products among health care professionals.
In principle the key definitions of “Biotherapeutic Product (BP),” “Similar Biotherapeutic Product (SBP)” and “Reference Biotherapeutic Product (RBP)” should be discussed and agreed by this subcommittee.

4. Product licensed and under existing process

TFDA has licensed the original biotherapeutic products based on evaluation of full dossiers on quality, non-clinical and clinical data. Those biotherapeutic products which have been subsequently licensed as biogeneric products were evaluated based on stand alone approach. This abbreviated stand alone approach-only requires full quality dossier and reduced clinical data based on non-comparative exercises.

5. Addressed issues

For those existing biotherapeutic products which have previously been approved and subsequently licensed for marketing in Thailand prior to full implementation of new regulation, they are subject to the re-evaluation process in order to be standardized under comparability exercises. However, it may take a few more years before TFDA is able to embark on a re-evaluation project for these biogeneric products as subsequently licensed biogeneric products. The new regulatory pathway for reviewing existing biotherapeutic products shall be based on the re-evaluation processes as follows:

1) The Quality aspect shall be based on the latest version of National or International Compendia or other relevant International Guidelines.
2) The Clinical aspect shall be based on clinical data of each therapeutic indication. Extrapolation of indication shall not be allowed unless being approved and justified by TFDA’s invited experts.
3) The Safety aspect shall be based on Post-Marketing Surveillance and/or Periodic Safety Update Report.
   - New drugs: Full quality, safety and efficacy dossier
   - Biogeneric: Quality plus reduced clinical dossier with non-comparative manner (Section 4). This product class would be converted to subsequently licensed biotherapeutic products after re-evaluation project will be completed.
   - Existing biotherapeutics (or subsequently licensed biotherapeutic products): Subject to re-evaluation (Section 5)
   - Similar biotherapeutical products: Comparative quality, reduced non-clinical and clinical dossier in comparative manner (similar to WHO guidelines)

6. Differences of Thai SBP guideline from WHO guidelines

We expect to use WHO guidelines as a basis for establishing regulatory frameworks for licensing of the similar biotherapeutic products as we aim to provide acceptable principles for licensing biotherapeutic products that are claimed to be similar to original biotherapeutic products of assured quality, safety, and efficacy, that have been licensed based on a full licensing dossier. On the basis of proven similarity, the licensing of a SBP will rely on full similar quality with head-to-head comparison and in part on non-clinical and clinical data generated with an already licensed reference biotherapeutic product (RBP), which is licensed in Thailand in principle.

7. Plan to implement SBP guideline

It is expected that in the near future within the year 2011, TFDA will be able to develop its own regulations based on the WHO’s guideline on evaluation of SBP. This new Regulation on SBP will be fully implemented by not only the National Regulatory Authority but also industries.

Conflict of interest

Prapassorn Thanaphollert: The author has disclosed no potential conflicts of interests.
Kriang Tungsanga: A co-investigator in a multi-center clinical trial of MIRCERA in CKD patients. The project was funded by Hoffmann-La Roche Ltd.