IFPMA Policy Position

26 July 2018

IFPMA Policy Position on Non-Comparable Biotherapeutic Products

The World Health Organization (WHO) Guidelines define similar biotherapeutic products (SBP) as "a biotherapeutic product which is similar in terms of quality, safety and efficacy to an already licensed reference biotherapeutic product" (RBP).[1] However, there are also products on the market that are intended to "copy" another biotherapeutic product but have not been directly compared against an already licensed RBP in a biosimilarity exercise as described in the WHO's Guidelines on evaluation of SBPs[1]. Yet, these medical products routinely share the same international non-proprietary name (INN). IFPMA uses the term "non-comparable biotherapeutic product" (NCB) to distinguish these products from SBPs.

National Regulatory Agencies (NRAs) emphasize the importance of comprehensive comparative development requirements including (a) quality, (b) safety, and (c) efficacy evaluations prior to regulatory approval and marketing, with robust pharmacovigilance post approval.[2,3] Evidence of a high degree of similarity to the RBP, from comparative, analytical and functional assessments, forms the basis of reduced non-clinical and clinical requirements and the expectation of similar efficacy and safety. In contrast, NCBs have not been compared in all three of these fundamental areas to a licensed RBP as defined by WHO guidelines, and therefore the clinical profile of NCBs may not necessarily be expected to be the same as the RBP and remains unknown.

There is an increasing number of publications indicating key quality differences and/or lack of analytical similarity between different NCBs and the RBP. [4,5] Considering that some NRAs are still in the process of adapting their regulatory frameworks for biotherapeutic products, some NCBs continue to be licensed under regulatory pathways that are not appropriate for biotherapeutic medicines.[6] This may put patients at risk with respect to expected clinical outcomes. As the global market is experiencing a considerable rise in the number of approved originator biotherapeutic and SBPs, actions must be taken to ensure patients have access to similar biotherapeutic products that meet WHO regulatory guidelines. Thus, IFPMA;

- believes that SBPs should not be approved as generics and require a distinct regulatory pathway consisting of comparative evaluation of quality, efficacy and safety in a manner consistent with WHO Guidelines[7];

---

[1] WHO Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs), P. 6: http://www.who.int/biologicals/areas/biological_therapeutics/BIOTHERAPEUTICS_FOR_WEB_22APRIL2010.pdf

[2] Dörner T, et al (2013) The role of biosimilars in the treatment of rheumatic diseases: Ann Rheum Dis 72:322-328

[3] Mellstedt H (2013) Anti-neoplastic biosimilars – the same rules as for cytotoxic generics cannot be applied: Annals of Oncology 24 (Supplement 5): v23-v28

[4] Park et all. J Pharm Sci. 2009 May;98(5):1688-99

[5] Neh Nupur, Nidhi Chhabra, Rozaleen Dash & Anurag S. Rathore (2018). Assessment of structural and functional similarity of biosimilar products: Rituximab as a case study, mAbs, 10:1, 143-158, DOI: 10.1080/19420862.2017.1402996

[6] Halim et al. Pharm Res 2013

[7] WHO Guidelines "Regulatory assessment of approved rDNA-derived biotherapeutics": http://www.who.int/biologicals/areas/biological_therapeutics/Annex_3_Regulatory_assessment_of_approved_rDNA-derived_biotherapeutics.pdf

International Federation of Pharmaceutical Manufacturers & Associations

Ch. Louis-Dunant 15
P.O. Box 195
1211 Geneva 20
Switzerland

Tel: +41 22 338 32 00
Fax: +41 22 338 32 99
www.ifpma.org

- supports an approach that will provide a framework for retrospective evaluation of products licensed prior to the establishment of a proper biotherapeutic and/or SBP pathway via supplementation with appropriate data in a timely manner consistent with the WHO rDNA product & SBP guidelines[8], while simultaneously ensuring that treatment of patients in the market is not interrupted;
- believes that NCBs should not be referred to as SBPs nor contain a copy of the RBP clinical data in their labels. NRAs may consider use of a symbol to indicate that similarity to the RBP has not been demonstrated;
- strongly supports the development of robust pharmacovigilance systems that support unique product identification to ensure the best possible traceability, including in regions where no infrastructure exists. Moreover, IFPMA recommends NRAs to encourage reporting practices amongst healthcare professionals, patients and their carers, especially while the NCB is being re-evaluated, and that mechanisms are in place, e.g. via naming, to continuously strengthen pharmacovigilance and to ensure the adequate traceability of adverse drug reactions.

[8] Guidelines on the quality, safety, and efficacy of biotherapeutic protein products prepared by recombinant DNA technology: http://www.who.int/biologicals/biotherapeutics/rDNA_DB_final_19_Nov_2013.pdf