INTERNATIONAL GENERIC PHARMACEUTICAL ALLIANCE

18 September 2013
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Professor John Skerritt
National Manager
Therapeutic Goods Administration

Delivered via email: John.Skerritt@tga.gov.au

Re: TGA Guidance titled "Evaluation of Biosimilars" posted on TGA website, 30 July 2013

Dear Professor Skerritt:

In an era when increasing demands are being made on the world's healthcare services, generic medicines provide a major benefit to society by ensuring patient access to quality, safe and effective medicines while reducing the cost of pharmaceutical care. The International Generic Pharmaceutical Alliance (IGPA) was born as an international network of generic medicines associations, committed to promoting generic medicines and exchanging information worldwide.

We applaud TGA's early adoption of biosimilars and commend your alignment with EMEA. You have consistently supported the industry and worked closely with our membership. However, it recently came to the attention of the IGPA that the TGA published a draft guidance entitled "Evaluation of Biosimilars" on its website[1] on the 30 July 2013). This draft guidance raises serious concerns for our Member Associations,[2] who collectively embody the global biosimilar medicines industry and especially those companies that serve highly regulated global markets and for patients seeking affordable biological medicines.

Based on a review of the Draft Guidance, the recommendations related to naming biosimiliars appear to follow the WHO ***draft*** biosimilar naming policy paper (INN Working Doc. 12.321/December 2012). It is proposed that all SBPs (biosimilar products) would bear a two part name:

[1] http://www.tga.gov.au/industry/pm-argpm-biosimilars-00.htm

[2] Members Include: Canadian Generic Pharmaceutical Association, European Generic medicines Association, Generic Pharmaceutical Association, Jordanian Association of Pharmaceutical Manufacturers, Japan Generic Medicines Association, and National Association of Pharmaceutical Manufacturers. •In addition, generic medicines associations from Brazil and Taiwan have observer status

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1. The first part of the name is the International Nonproprietary Name (INN) of the reference product. This addresses the transparency of the identity of the reference product.
2. The second part is an SBP identifier, composed of the prefix sim and a random fantasy suffix which conforms to the INN naming principles, thus clearly distinguishing the SBP from the reference product and also from all other SBPs.

IGPA has serious concerns about the naming recommendations put forth in the above referenced draft guidance. Naming of biosimilars represents a major issue for access to high quality, affordable biological medicines for patients. Naming should be based on consistent scientific principals as it has been for decades. Further, the lack of global consistency for naming of biosimilars will result in a loss of scientific basis for naming, confusion and uncertainty for practitioners and patients and inappropriately delayed access to affordable biologicals. Global naming inconsistency also hampers global pharmacovigilance activities.

SCIENCE

IGPA believes that unique names for biosimilar products that are intended to be highly similar to the reference product fail to adhere to sound science. Highly regulated regions have used comparability approaches for nearly two decades to allow originator companies to make changes to an existing product. These changes, such as, cell lines, processes, new facilities, etc., result in the originator product being 'comparable' or highly similar to the original version. Yet, regulators did not see a need for differentiating pre-change and post-change products with unique names. In the event of such changes, originators must demonstrate comparable safety and efficacy. To an even greater degree, SBP applicants must establish comparable safety/efficacy and therapeutic equivalence to the originator product, and must have essentially the same labelling as the originator product.

As mentioned, science should be the grounding basis for nomenclature. The science of comparability is well established and allows regulators to approve SBPs using the same scientific approaches as those used for originators when changes are made to the product after approval. Originators have used the ICH Q5E Guideline on comparability of biotechnology products, among other regional guidances, to establish comparability after manufacturing changes; hence the science is well established.

Now, with the advent of SBPs, originators have been actively seeking strategies to inhibit competition and availability of affordable biological products. To be clear, nomenclature for SPBs is not addressed as a critical aspect for SBPs in the laws of any highly regulated regions, or indeed anywhere in the world. However, as the originator industry failed to convince lawmakers of the need to ensure SBPs were allocated unique names, originators have now initiated a concerted global effort to thwart competition by creating policy obstacles to marketing SBPs by (amongst other things) heavily promoting the need for unique names in spite of a complete lack of objective data to support the need for unique names.

EXPERIENCE

IGPA is very concerned that the TGA has made this decision, which is inconsistent with other global regulatory bodies, such as the EMA, who has the most significant global biosimilar experience. Moreover, the EMA biosimilar policies and processes are based on its successful track record with the thirteen currently licensed biosimilar products on the market. It is also important to note that there have been no reported cases of misidentification or failure of pharmacovigilance systems due to the INN name for the biosimilars being the same as for the reference product. The first two monoclonal antibodies have also just been approved in the EU with the same INN as their reference product Remicade®. TGA has experience with biosimilars also, three Filgrastim biosimilars on the market with the same INN. There is no good reason to change policy and no good reason for to diverge from the current position.

Additionally, the introduction of biosimilar/SBPs should not result in unique pharmacovigilance changes that are different from those applied to other pharmaceuticals. SBPs will be approved based on sophisticated analytical comparisons to the originator product along with requisite safety and efficacy information. This is essentially the same approach as addressed in the ICH Q5E guideline which is relied upon by originators (with no requisite prefix or suffix to identify the changed product). A suffix to the INN is **not** required to provide product identification and may actually introduce confusion or medication error. Additionally, the confusion will diminish the utilization of affordable SBPs and deprive patients of affordable biological medicines. IGPA recommends that TGA should reverse its position on requiring a unique suffix for biosimilars and when a SBP is deemed to be biosimilar, the same INN should be used.

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SYSTEM

Formal didactic and experiential training of clinicians relies heavily on the utilization of consensus practice guidelines and treatment algorithms supported by evidenced-based medicine for the selection of therapy for management of diseases/conditions. To this end, the utilization of consensus practice guidelines has become foundational; providing physicians and other health care providers, health plans, integrated delivery systems, purchasers, and others an accessible mechanism for obtaining objective, detailed information on clinical practice recommendations and level of evidence substantiating the practice. Several organizations globally are committed to this effort to ensure consistency of clinical practice recommendations. In the context of these guidelines and treatment algorithms, therapies are identified by INN nomenclature that does not include unique names when products have demonstrated that they are the same. The combination of harmonized consensus guidelines and consistency of INN nomenclature across national and international names permits a common language for clinicians to communicate therapeutic intent and to effectively track safety and effectiveness. As such, the utilization of the same INN for a biosimilar medication, as the originator biologic, allows for ***clarity of therapeutic intent*** across the continuum of health care professionals involved in the prescribing, dispensing and administration of biologic therapeutics in accordance with consensus guidelines.

As a further point of clarification, the only time a full suffix has been employed in the nomenclature of biologic therapeutics conventional has been the utilization of a Greek letter in full suffix to address differences in glycosylation patterns, pharmacologic activity and therapeutic intent (e.g., interferon-alfa, interferon-beta, etc.). Importantly, these Greek suffixes connote to clinicians distinct therapeutic entities and NOT SBPs that are intended to have exactly the same conditions of use as the originator product, and in certain cases reflect distinct mechanisms of pharmacologic activity. In the case of interferons with Greek letter in full suffix, the nomenclature provides distinction between therapeutic proteins with different therapeutic utility.

Conversely, using a full suffix when it is not for purposes of differences in glycosylation patterns, pharmacologic activity and therapeutic intent can lead to confusion and create barriers to market access. This has been the experience in Europe where one biosimilar product has a different INN; epoetin zeta vs. epoetin alpha has caused significant confusion and created barriers to market access including national tenders in countries such as Italy. Assigning unique ABNs to biosimilars/SBPs will not improve the risk benefit ratio for patients, but it will cause confusion in the market place in Australia or other parts of the world. Rather, based on several years of actual use of SBPs in the EU, use of the same INN for SBPs has not raised the very concerns that are being promoted by special interest groups.

Consideration has been given to the use of a suffix to identify the manufacturer, 'appended' to the INN for biosimilars. This approach may also introduce confusion in the continuum of appropriate prescribing, dispensing and administration of a biologic product. This convention would require the health care community to be fully versed with the myriad of manufacturers for biologic therapeutics and permutations of manufacturer suffixes with over-specification of the product naming, potentially leading to delay in product administration to the patient if the exact match of nomenclature was not consistently applied throughout the prescribing-dispensing-administration communication chain. This over-specification would inadvertently introduce perceived distinction across biologics with demonstrable evidence of analytical similarity, bioequivalence or therapeutic equivalence requisite for the approval of biosimilar medications. The fundamental prescribing practices are predicated on consensus guidelines and INN naming to ensure clarity of therapeutic intent for pharmacotherapeutics inclusive of small molecules and proteins. Guidelines are silent to manufacturer attribution. Requiring suffixes as integral to the nomenclature for biosimilars would create confusion by employing a level of specificity that connotes differentiation when evidence does not support such distinction for biosimilars consistent with originator biologic therapies.

Instead, to avoid confusion and mitigate medication error, biosimilar therapeutics could be identified by a unique proprietary name (brand/trade name). This unique name, coupled with the same INN as the originator biologic, would provide the differentiation desired without creating confusion for the healthcare professionals. Prescribing biologics by brand/trade name is a long standing practice in Europe and has not changed with the market entry of biosimilar medicines. Furthermore for adverse drug reporting, the brand name and the lot number must be communicated. This requirement is now enshrined in the new EU Pharmacovigilance legislation.

The long standing WHO and regulatory body scheme for naming originator drugs and their therapeutic equivalents has worked well over 40 years of history. No specific safety issues with biosimilars/SBPs have been identified using the existing INN naming convention. It is the view of the IGPA and the global generic

and biosimilar pharmaceutical industry that introduction of an additional unique ABNs on top of unique brand/trade names will only create confusion and complexity for patients and healthcare professionals alike.

The IGPA requests that any final guidance by TGA on evaluation of biosimilars include the recommendation to utilize the same INN as the originator to reflect that the SBP has been determined to be highly similar.

Respectfully submitted,

IGPA Member Associations

CGPA EGA Making Medicines Affordable GPhA JAPM JGA NAPM