Specialty Healthcare Benefits Council
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"A Rose by Any Other Name…": Imperatives for Biosimilar Naming

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With apologies to William Shakespeare's famous quote as Juliet contemplates the importance of a name, one of the emerging issues surrounding the development of biosimilar medications is what to call them. How these agents are ultimately named affects multiple elements of their use including safety, tracking, billing, promotion, and information dissemination. Even the category, biosimilars, causes naming confusion with terms like generic biopharmaceutical, biogeneric, follow-on protein, subsequent entry biologics, biosimilar, and follow-on biologic all in use to refer to these agents.[1] For clarity, this article will use the term biosimilar to categorize these agents.

Biosimilars, like their innovator products, are biologic agents in which the active drug is produced by or derived from a living organism. This is accomplished by gene expression or recombinant DNA techniques. In general, a biosimilar is a biopharmaceutical or other biological product whose patent protection has expired and can now be made by a company different from the originator of the product. The process to make the biosimilar can be the same as or different from the originator, but the end product has to be comparable or bioequivalent to the originator product as determined by the US Food & Drug Administration (FDA).

Biosimilars Versus Generics

Before considering naming options, it is important to distinguish biosimilars from typical generic medications. Generic pharmaceuticals are composed of small molecules which are relatively easy to manufacture. Virtually exact chemical replicas of the originator product can be produced. These generic drugs are considered to be the same as the originator product for all practical purposes. In contrast, biosimilars are made of highly complex proteins which are thousands of times larger than their small-molecule generic counterparts and are manufactured through much more complex molecular cloning and fermentation techniques. Biosimilar manufacturers are not able to see the originators' processes and can't access their active pharmaceutical ingredients, cell banks, fermentation, or other processes. Any slight deviation in these processes has the potential to cause significant issues with the clinical impact and performance of the products. It is easy to see that biosimilars, although similar, as the name suggests, cannot really be considered generics in the same sense as small molecule products, and this leads to issues in naming these products.[2]

Official Names

Innovator products almost always have trade names assigned by the manufacturer. These are registered trademarks that are owned by the manufacturer and are exclusive to the originator product. Trade names cannot be extended to their biosimilar counterparts. Of greater interest is the United States Adopted Name (USAN). The ultimate selection of a name by the FDA generally involves the adoption of a USAN. This is the non-proprietary, or generic, name for a drug. The USAN is assigned by the American Medical Association (AMA). The United States Pharmacopeia (USP) public standards are also an important element for naming drugs, as they help ensure consistent identity, potency, purity, and quality of off-patent medications.[3] USP is also a stakeholder in naming because its monographs link a product to the non-proprietary name in a monograph chapter. It is also important to note that USP standards are considered enforceable by the FDA for purposes of determining adulteration or misbranding.[4] No matter the ultimate USAN, each product is marked by a unique National Drug Code (NDC). This is generally an 11-digit code that allows identification of the drug, dosage, packaging, and manufacturer.

FDA

The FDA is keenly aware of the significance of the development of biosimilars and has released 3 biosimilar guidances.[5] To date the FDA has not taken an official position on biosimilar naming convention. However, the naming for 2 new biologics related to previously approved products (Zaltrap & Neutroval) may provide some insight into the FDA's naming preference. For these agents the FDA assigned unique non-proprietary names. They added a prefix and hyphen to a root non-proprietary name, giving us ziv-afilbercept and tbo-filgrastim. In adopting this position, the FDA indicated that a non-proprietary name distinct from the previously approved and structurally related products would help minimize error by preventing wrong product selection, preventing confusion with interchangeability, and facilitating post marketing safety monitoring by ensuring a clear means of identifying which product was dispensed.[6]

When considering a long-term position for biosimilar naming, 3 potential strategies stand out.

- *A common non-proprietary name:* The innovator and biosimilar products share a common non-proprietary name while the unique NDC is used as the mechanism to identify the product and manufacturer.
- *Shared root or prefix:* A non-proprietary name with a shared root is used but a distinct prefix to identify the product and manufacturer is added.
- *Distinct non-proprietary name:* An entirely distinct non-proprietary name is given for each product.

Each of these options has positive and negative factors associated with its use. However, it must never be forgotten that the most important element of the naming debate is patient safety. The foundational element of biosimilars or any medication is patient safety and at the core of the FDA process is the assurance that products approved for use are first and foremost safe and effective. Whatever the final configuration, the biosimilar naming process should be a viable, long-term solution focused on safety. The name should help improve safety by having the following attributes:

- Differentiating the product from others,
- Avoiding "sound-alike" errors,
- Allowing for effective tracking/tracing of products, and
- Ensuring that adverse events can be attributed to the correct product.

Common Non-Proprietary Names

There is support for the use of a common non-proprietary name between biosimilars and the innovator product. Four major pharmacy organizations, The American Pharmacists Association (APhA), the National Association of Chain Drug Stores (NACDS), the National Community Pharmacists Association (NCPA), and the Academy of Managed Care Pharmacy (AMCP), have provided position papers to the FDA supporting this naming convention.[7,8] The general consensus in these organizations is that use of a common non-proprietary name could reduce confusion among prescribers and patients as well as facilitate substitution, where appropriate. On the other hand, there is concern that unique non-proprietary names for common active ingredients could contribute to confusion among prescribers and pharmacists, thereby increasing the chance for a medication error. It is also felt that unique non-proprietary names may make it more difficult to easily determine which products are biosimilar and interchangeable with innovator products, which could lead to therapeutic duplication. The major issue with this approach appears to be an increase in the difficulty of tracking the specific product that a patient receives to ensure that any safety monitoring concerns are correctly attributed to the right product and manufacturer.

The NDC code has been proposed as the primary tracking tool. While this approach would be theoretically possible, in actual practice it presents several problems. Although NDCs are useful, relying on them as the primary means of identification would be problematic in reporting or recording information, for the following reasons:

- People use names and not NDCs when recording drug information in records.
- If bar codes are used, not all systems actually capture and record the NDC.
- Manually recording the NDC for the millions of doses an organization typically administers annually would be a very labor-intensive process.
- A significant amount of data is generated from medical claims which do not uniformly require NDCs.
- NDCs are rarely on Rx labels.
- With up to 11 digits, NDCs are prone to errors.

Shared Root and Prefix Naming

Under this naming configuration, biosimilar and innovator products would share a common root linking the products, but a unique prefix would be added to differentiate each product and manufacturer. Having a shared root

and distinct prefix in the non-proprietary name would serve to demonstrate a clear relationship between the reference and biosimilar products but would still be able to differentiate the biosimilar from the reference drug. This would definitely assist with product and manufacturer identification. However, this approach would not necessarily support an easy pharmacovigilance program. In fact, it could make it more difficult to collect global safety and quality data on similar therapeutic drugs.

Distinct Non-Proprietary Name

A third option is to consider having an entirely distinct non-proprietary name for each biosimilar product. This approach would ensure that biosimilar and reference products would not be confused with each other. It would also assist in easily tracing and identifying the product manufacturer. However, having distinct non-proprietary names would provide no indication that products are related, which may create issues when searching for "class effects." In addition, distinct names could possibly contribute to mistaken therapeutic duplication.

SUMMARY

The issues of biosimilars are very complex, and it is clear that there will be a definite learning curve as more agents reach this stage of development and are approved for use. There is no easy answer for naming configurations, but patient safety should be the overriding concern for all parties when selecting a final biosimilar naming configuration. Manufacturers, patients, government, and professional organizations should work together to reach a final solution that is supported by comprehensive programs for education and awareness covering how best to prescribe, dispense, and use these products.

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