Novartis Position on Biosimilars – Key Regulatory and Market Access Aspects

GPP 301.V1.0.EN

The mission of Novartis is to discover new ways to improve and extend people’s lives. Using science-based innovation, Novartis delivers better outcomes for patients and addresses the evolving healthcare needs of society.

One of the company’s focus areas is the growing class of biological medicines (“biologics”)\(^1\). Biologics bring significant medical benefit to patients, specifically in areas such as cancer and auto-immune diseases. Biosimilars are biologics that are approved on the basis that they are highly similar to a previously approved biological medicine (the reference product). Biosimilars have no clinically meaningful differences to the reference product in terms of quality, safety and efficacy. They can be launched after loss of exclusivity of the reference product\(^2\).

Biological medicines manufactured by use of biotechnology have been approved by regulators and used by doctors and patients since the early 1980s. In 2004, Europe was the first region to establish a specific market authorization pathway for biosimilars. Since then, many countries have established specific legislative frameworks and regulatory pathways for development, registration and market access of biosimilars. Unlike for the development of generics, a clinical safety and efficacy study is typically required for biosimilars to confirm biosimilarity to the reference product.

In 2010, the United States established a legal framework for regulatory approval of biosimilars. In addition to establishing U.S. standards for biosimilarity, the law includes a unique approach by creating a specific designation for interchangeable biosimilars. No other country has a separate "interchangeability" designation. The ability to obtain an FDA designation of interchangeability will require that the sponsors provide an additional set of data. This data should establish that the clinical outcomes will be the same as the reference product in any given patient and that safety and efficacy are not impacted when switching between the reference product and the biosimilar\(^3\)\(^4\). An interchangeable biological product may be substituted for the reference product by a pharmacist without the intervention of the healthcare provider who prescribed the reference product\(^5\).

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\(^1\) For the purpose of this document biological medicines are defined as large molecule medicines that are grown in- or derived from living organisms.

\(^2\) For more information on biosimilars, visit [https://www.sandoz.com/biopharmaceuticals](https://www.sandoz.com/biopharmaceuticals)

\(^3\) As of the effective date of this position, guidance on interchangeability has not yet been released by the FDA

\(^4\) Section 351(k)(4) of the Public Health Service Act

\(^5\) Section 351(i)(3) of the Public Health Service Act
Novartis Position

Novartis is committed to improving lives of patients through both innovative biologics and increased access to treatment through the introduction of biosimilars.

Drawing upon our unique and significant experience in both originator biologics and biosimilar development and commercialization, Novartis supports the following principles for a science-based approval pathway and market access principles for biologics including biosimilars:

1. Extrapolation

Extrapolation of indications should be based on totality of evidence.

Regulatory guidelines for approval of biosimilars allow for extrapolation of indications. The concept foresees that all available biosimilar data and reference product knowledge are utilized to obtain approval for use of the biosimilar for other indication(s) of the reference product's label.6

Novartis supports extrapolation based on the totality of evidence generated during the development process. Therefore, not only data should be integrated from clinical but also comparative analytical and pre-clinical studies including knowledge on the mechanism of action and any other factor that may affect the safety and efficacy in each indication.

2. Labeling

A biosimilar should have the same label as the reference product.

Novartis supports the use of the same wording for a biosimilar label as the reference product's label; including the data provided to support the expected efficacy and safety. In the event however, that the approved indications, presentations, or administration device of a biosimilar are different from the reference product, the label should reflect this additional information.

3. Naming

A biosimilar should have the same international nonproprietary name (INN) as the reference product.

A biosimilar product should have the same INN as the reference product.

An additional suffix to distinguish different biologics with the same INN or biosimilars from their reference products is not necessary. Experience with existing commercially available biologics, including biosimilars, that share non-proprietary names, shows that these products are adequately distinguished by existing identifiers, e.g. their brand name7 8. In contrast, we believe that new naming systems that deviate from well-established systems for all other pharmaceuticals may lead to treatment errors by introducing unnecessary complexity into the pharmacovigilance system. They may therefore have serious consequences for patients, healthcare providers and healthcare systems.

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6 EMA nonclincil guideline Rev1/2015; FDA general biosimilar guideline 2014; WHO 2009
4. Regulatory interchangeability designation

There is no scientific need for a regulatory interchangeability designation.

Novartis believes that there is no scientific need for an additional regulatory interchangeability designation after biosimilarity has been established. To ensure robust regulatory pathways, regulatory authorities should follow the World Health Organization (WHO) "Guidelines on evaluation of similar biotherapeutic products", or guidelines of the European Medicines Agency (EMA). Under these guidelines, biosimilars are approved only when the products have been demonstrated to be essentially the same as the reference product in terms of safety, efficacy and quality. The introduction of an additional step in the regulatory review process to establish interchangeability adds additional complexity and costs – for both manufacturers and regulators – with no relevant patient benefit or impact on efficacy or safety.

Interchangeability in the US

All approved biosimilar medicines in the US meet FDA's requirements, demonstrating there are no clinically meaningful differences in terms of safety and efficacy to the reference product.

Novartis believes that an FDA determination of interchangeability would be a confirmation that the risk of alternating or switching between the biosimilar and the reference product is no greater than the risk of using the reference product only. The FDA's determination of interchangeability does not represent a higher standard of product quality.

5. Switching

Under the guidance of a physician, patients can be transitioned from a reference product to a biosimilar.

Biosimilars are developed to be highly similar to their respective reference products and are approved as having no clinically meaningful differences in terms of safety, efficacy and quality. Under guidance of a physician – with a treating physician being the best suited individual to make this decision - patients treated with a reference product can be safely transitioned to a biosimilar.

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