

Novartis Position on innovative Biologic Medicines and Biosimilars

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 biologic medicinesⁱ. Biologic medicines bring significant medical benefit to patients, specifically in areas such as cancer and auto-immune diseases. Biosimilars are biologic medicines that are developed to match their reference medicine in terms of safety, efficacy and quality and are approved as having no clinically meaningful differences to the reference product. They can be launched after loss of exclusivity of the reference biologic medicineⁱⁱ.

Biologic 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 biosimilar medicines. Since then, many countries have established specific legislative frameworks and regulatory pathways for development, registration and market access of biosimilar medicines. Unlike for the development of generics, a clinical safety and efficacy study is typically required for biosimilar medicines to confirm biosimilarity to the reference product.

In 2010, the United States established a legal framework for regulatory approval of biosimilar medicines. In addition to establishing U.S. standards for biosimilarity, the law includes a unique approach by creating a specific designation for interchangeable biosimilar medicines. No other country currently 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 medicine.

Novartis position

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

Drawing upon our unique and significant experience in both innovator biologic and biosimilar development and commercialization, Novartis supports the following principles for a science-based approval pathway and sustainable market access for biologic medicines:

1. Extrapolation

Extrapolation of indications should be based on totality of evidence.

Regulatory guidelines for approval of biosimilar medicines 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 medicine in other indication(s) of the reference product's label.ⁱⁱⁱ

Novartis supports extrapolation based on the totality of evidence generated during the development process, including comparative analytical, pre-clinical and clinical data as well as any other factor that may affect the safety and efficacy in each indication, such as the mechanism of action.

2. Labeling

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

Novartis supports the use of the same wording for a biosimilar label as the reference medicine'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 medicine are different from the reference biologic medicine, the label should reflect this additional information.

3. Naming

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

A biosimilar medicine should have the same INN as the reference biologic medicine.

An additional suffix to distinguish different biologic medicines with the same INN or biosimilar medicines from their reference biologic medicine is not necessary.

Experience with existing commercially available biologic medicines, including biosimilar medicines that share non-proprietary names, shows that these products are adequately distinguished by existing identifiers, e.g. their brand name.^{iv,v} 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.

4. Regulatory interchangeability designation^{vi}

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, biosimilar medicines are approved only when the medicines have been demonstrated to be essentially the same as the reference medicine in terms of safety, efficacy and quality. The introduction of an additional step in the regulatory review process to establish interchangeability adds additional complexity, time and costs – for both manufacturers and regulators – with no relevant patient benefit or impact on efficacy or safety.

Interchangeability in 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 medicine.

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 medicine is no greater than the risk of using the reference medicine only. The FDA's determination of interchangeability does not represent a higher standard of product quality.^{vii}

5. Switching^{viii}

Under the guidance of a physician, patients can be switched from a reference medicine to a biosimilar.

Biosimilars are developed to match their reference biologic medicine in terms of safety, efficacy and quality and are approved as having no clinically meaningful differences to the reference product.

Under the guidance of a physician- with a treating physician being the best suited individual to make this decision - patients treated with a reference medicine can be safely switched to a biosimilar.

Switching between biosimilars

In stringent regulatory systems, biosimilar medicines are developed to match their respective reference biologic medicines and are approved as having no clinically meaningful differences. As a consequence, under the guidance of a physician, a patient can be switched to a biosimilar medicine, back to the reference medicine and, we believe, from one biosimilar medicine to another.

6. Procurement of biologic medicines

Novartis supports competition by biosimilar medicines to allow health systems to invest savings from procurement of off-patent medicines in expanding access to treatments and innovative therapies.

Manufacturers of innovator and biosimilar medicines should have equal opportunities to secure treatment volumes based on the overall value^{ix} of the medicine for patients and the health care systems. Market intervention tools that unilaterally favor one product class should not be promoted. Disincentives to the use of biosimilars should be removed.

Participation of multiple players in the market (reference biologic and biosimilar medicines) is preferable to a “winner-takes-all” approach, which discourages both reference biologic and biosimilar medicine manufacturers from staying in the market in the long term.

Policies to promote the use of biologic medicines need to address additional issues compared to frameworks for generic small molecules. In particular, biologic medicines require specific pricing and market access considerations that reflect the comparably higher regulatory and manufacturing complexities as well as the significant value they bring to patients and society. Specificities of each therapy area and biologic molecule should be taken into account.

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ⁱ For the purpose of this document biologic medicines are defined as large molecule medicines that are grown in or derived from living organisms.

ⁱⁱ For more information on biosimilars, visit www.sandoz.com/biosimilars.

ⁱⁱⁱ EMA nonclin/clin guideline Rev1/2015; FDA general biosimilar guideline 2014; WHO 2009.

^{iv} Stergiopoulos S, Brown CA, Gramp G, Felix T and Getz KA. Identifying and Quantifying the Accuracy of Product Name Attribution of US-Sourced Adverse Event Reports in MedWatch of Somatropins and Insulins. *Therapeutic Innovation and Regulatory Science*. 2015. 49(5): 706-716.

^v Novartis submission to the FDA Draft Guidance “Nonproprietary Naming of Biological Products”, August 2015. FDA-2013-D-1543-0172, page 7.

^{vi} Outside of the United States. Definition of interchangeability in EU: The medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient of the initiative, or with the agreement of the prescriber [EC consensus document, “what you need to know about Biosimilar products”](#)).

^{vii} FDA draft was issued in January 2017. No product has yet been granted this designation.

^{viii} Switching: Decision by the treating physician to exchange one medicine for another medicine with the same therapeutic intent in patients who are undergoing treatment [EC consensus document, “what you need to know about Biosimilar products”](#)).

^{ix} value is defined as clinical, patient, health care system and societal value.