PUBLIC POLICY STATEMENT

Biosimilars

Biologics have revolutionized the treatment of patients suffering from some of the most debilitating and life-threatening diseases. A biosimilar is a biological medicine that is designed and demonstrated to be highly similar to the reference biological medicine according to established regulatory standards, such as the guidelines issued by the WHO, EMA and FDA. As with any medicine after expiry of data and market exclusivity of their reference medicine, biosimilars provide additional treatment options and offer savings to health systems due to competition between multiple manufacturers.

Biologics are complex proteins derived from living sources and are generally more complex than small-molecule drugs. Due to the specific development and manufacturing process for biological products, a biosimilar cannot be "identical" to its reference product, as is the case for small-molecule generics. Biosimilar policies must therefore reflect the specificities of biologics, particularly regarding switching and substitution, naming, pharmacovigilance, and procurement practices.

Merck believes patient health outcomes are best served by aligned science-based regulations. We support legislation and administrative practices that sustain robust regulatory frameworks for biologics, including biosimilars, that are aligned with WHO guidance and international best practice. We encourage national and regional health authorities to undertake work sharing and reliance measures to achieve efficient and effective outcomes for patients.

Approval: A biosimilar is not regarded as a generic of a biological medicine. This is mostly because the natural source, variability, and more complex manufacturing of biological medicines do not allow an exact replication of the molecular micro-heterogeneity. Over 15 years of experience of biosimilar regulatory review, approval, and use globally has confirmed the value of established biosimilar guidelines from the WHO[1], EMA[2], and FDA[3] and related guidelines in countries around the world. Although scientific progress and experience has introduced new analytical techniques and production technologies to advance biosimilar development and assessment, the cornerstone remains that robust evidence is required to support the decision to license a biosimilar and this totality of evidence must ensure that the biosimilar candidate demonstrates similarity in quality, safety, and efficacy to the reference product within clinically acceptable ranges.

Naming: Unlike with small-molecule generics and because of the specificities of biological medicines, we support regulatory systems like in the European Union that ensure clear

[1] https://www.who.int/publications/m/item/guidelines-on-evaluation-of-biosimilars
[2] Biosimilar medicines: marketing authorisation | European Medicines Agency (europa.eu)
[3] https://www.fda.gov/vaccines-blood-biologics/general-biologics-guidances/biosimilars-guidances

identification of a prescribed biological medicine and effective traceability for pharmacovigilance.[4,5] This requires that at least the brand name and the batch number are tracked and that prescriptions of biological medicines also include the brand name.

Prescription: Recognizing that physicians and patients are in the best position to make the right treatment decision, the physician must always have the authority to decide with the patient, which version of a biological product is dispensed to the patient. Moreover, this practice ensures that the patient health record captures the correct medicine used for effective pharmacovigilance.

Pharmacy substitution has been envisaged conceptually (sometimes embedded in national law) in a very rare number of instances and implemented in even fewer instances. In such situations at least the following criteria must be met:

- Clear and transparent regulations by a National Regulatory Agency, supported by clinical decision makers or based on scientific evidence, have been established to permit the substitution of biological medicines at retail pharmacy level and allowing the prescribing physician a 'right-to-refuse' if justified for medical considerations;
- Adequate pharmacovigilance systems are in place to facilitate product tracking and the rapid and accurate identification of the dispensed product (see "Naming"); and
- The substitution is accompanied by the timely communication to the prescribing physician, as well as the patient or patient's representative.

Competition and procurement: The potential for significant savings to national health care systems clearly exists with the introduction of biosimilar products following the end of data and market exclusivity. Merck believes that the market for originator and biosimilar medicines should reflect prescription policies, patients' safety and health outcomes, and sustainable competition.

The participation of multiple manufacturers in the market following the introduction of biosimilars (reference biologic and biosimilar medicines) ensures the availability and sustainability of multiple treatment options. Any procurement approach should therefore allow for more than one treatment option so that a degree of physician and patient choice is ensured, and that the marketplace remains sustainable. In contrast, a "winner-takes-all" approach may risk forcing patients to be switched from their current treatment without alternatives and discouraging both reference biologic and biosimilar medicine manufacturers from staying in the market. Sustainable competition within a market following biosimilar introduction drives both continued investments to discover and develop future innovative biological products and savings for healthcare systems.

[4] See e.g. Directive 2010/84/EU amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use; Art. 102(e)

[5] OJ L 356/68-70 (22.12.2012), Commission implementing Directive 2012/52/EU of 20 December 2012 laying down measures to facilitate the recognition of medical prescriptions issued in another Member State; Recital 4