FAQs on Biosimilars

1. What are biologic medicines?

Biologics are medicinal products produced in living organisms. Unlike small molecule chemical medicines such as paracetamol, for which the manufacturing process can be replicated to produce an identical copy (“generics”), biologics are large complex molecules produced by living cells through highly specific processes. Even a slight change in the manufacturing process can vary the structure of the biologic compound and consequently impact the efficacy, safety and quality of the biologic medicine.

2. What are biosimilar medicines?

Biosimilars are “follow-on” versions of innovator biologic medicines. These “follow-on” versions are required to demonstrate similarity in physical and chemical characteristics, biological activity, safety and efficacy to the first approved biologic medicine, also referred to as the reference biologic product (RBP). The route of administration, dosage form and the strength of the biosimilar product should be same as the RBP. Biosimilar product is not identical but similar to the RBP.

3. How are biosimilar products approved?

Biosimilar products are required to go through a scientifically rigorous pathway based on a stepwise head to head comparability to the RBP in terms of quality of product (physical and chemical characteristics), non-clinical studies (toxicity, functionality) and clinical studies (safety, efficacy & immunogenicity). The comparability is designed to show similarity and demonstrate that there are no clinically meaningful differences between the RBP and biosimilar product.

A biosimilar product may ride on the safety and efficacy of the RBP to obtain approval for one or more indications approved for the RBP without head-to-head comparison in clinical studies for each indications. This is based on the overall evidence taking into account the physicochemical similarity demonstrated through analytical and functional assays (structure, molecular weight, binding assays, etc) that the biosimilar works in the same way as the RBP, as well as clinical studies conducted in the most sensitive clinical setting which allows the bridging of the efficacy and safety to other indications.

4. Can a biosimilar be used interchangeably with the RBP?

Interchangeability means the ability to change patient’s treatment between the RBP and the biosimilar, while achieving the same treatment response and safety profile in each individual patient.
A biosimilar should be comparable to the RBP in efficacy and safety, although their clinical effects may not be identical. To demonstrate that interchanging between RBP and the

biosimilar does not change the clinical response in the individual patient, specific clinical studies need to be conducted. These involve patients receiving initial treatment of either the RBP or the biosimilar and subsequently crossing over to the other treatment. Patients are then assessed if the clinical effect achieved by the initial treatment is maintained after crossing over to the subsequent treatment. Not all companies may conduct interchangeability studies. Please refer to the package insert of approved biosimilars for information on the relevant clinical studies. The package inserts are available on HSA website.

If a clinician wishes to change a patient's treatment to a biosimilar, careful monitoring of clinical response of the individual patient is advised.

5. What are the biosimilars approved in Singapore?

Biosimilar	RBP	Active ingredient	Approval date
SciTropin A	Genotropin	Somatropin	March 2009
Nivestim	Neupogen	Filgrastim	July 2012
Zarzio	Neupogen	Filgrastim	March 2015
Basaglar	Lantus	Insulin glargine	August 2016
Remsima	Remicade	Infliximab	March 2016
Truxima	Mabthera	Rituximab	April 2019
Amgevita	Humira	Adalimumab	July 2019

6.What are the important information required when reporting adverse events (AEs) associated with biosimilars?

It is important to provide the **brand name** *and* **batch/lot number** of the biosimilar in the AE reporting form. Other important information to report include:

- The patient's age, gender and medical history;
- Dose of biosimilar, its indication and treatment dates;
- Description of the AE, its onset date and outcome; and
- The reporter's profession and contact number.

Due to the characteristics of biologic medicines (see Q&A 2 & 3), a biosimilar product is similar but not identical to the RBP. Minor variations in the production process of a biologic medicine could lead to variability between different batches/lots of the same product. Hence, clear identification in terms of the **brand name** and **batch/lot number** of the product associated with the AE is important to facilitate identification of AEs that may be attributed to a specific brand or batch/lot of the product.

7. What are the post-marketing measures put in place to monitor the safety of biosimilars?

The current post-market vigilance systems for detecting safety issues relating to RBPs are applicable to biosimilars. These may include:

- Reporting of serious AEs associated with biosimilars to HSA by product registrants or healthcare professionals;
- Timely update by product registrants on significant safety issues and safety-related regulatory actions taken by overseas agencies;
- Submission of benefit-risk evaluation reports relating to the biosimilar by product registrants (when required);
- Conduct of post-marketing safety studies by product registrants (when required).

Risk minimisation activities to mitigate the risks known to be associated with RBPs will generally be adopted for biosimilars. These may include:

- Warnings and precautions in package inserts (e.g. warning statement on the risks associated with switching of products during treatment);
- Provision of educational materials for physicians and/or patients (when required).