DIGESTIVE CANCERS EUROPE

Frequently Asked Questions and Answers around Biosimilars

1. What are biological medicines?

Biological medicines (or biologics) are medicines that are made of one or more active substances produced by cells or organisms. They are used to treat different conditions including diabetes, psoriasis, rheumatoid arthritis, inflammatory bowel disease and cancer. Biologics have a larger, more complicated structure than traditional chemical medicines; generally, they cannot be made as pills and are administered by injection or an intravenous drip. In addition, the manufacturing process of biologics is longer and more complex than that of traditional chemical medicines leading to higher costs.

2. How are biologics monitored for safety and efficacy?

The European Medicines Agency (EMA) has a well-established system for monitoring, reporting, assessing and preventing adverse drug reactions for all medicines, known as pharmacovigilance practices. These practices include specific guidelines for biologics. The benefit-risk balance for all medicines (including biologics) is continuously evaluated. Whenever needed, necessary regulatory actions to safeguard public health, such as introduction of a new warning in the product information, restricting use or even removing a product from the market, are introduced.

3. What is a biosimilar medicine?

According to EMA, a biosimilar medicine (or biosimilar) is a biological medicine highly similar to another biological medicine already marketed in the EU - the reference medicine or originator. In other words, the active substance of a biosimilar is a version of the active substance of an existing product.

4. Why are biosimilars not considered to be identical to the originator medicines?

Biosimilars and originators (both known as biologics) are large and complex molecules made by cells or organisms. However, the production of biosimilars does not follow the same manufacturing procedure as that of the originator product because of patenting restrictions; thus, biosimilars cannot be identical to the originator. It should be noted however that a degree of variability is an inherent characteristic of all biologics (including biosimilars). As a result, different batches of the same biologic may have some subtle differences. However, all these differences – both between batches as well as between originators and biosimilars - are kept within strict limits without compromising the safety and efficacy of the particular medicine.

5. How are biosimilars developed and approved in the EU?

Biosimilars are manufactured following strict quality requirements, using state-of-the-art methods. Manufacturing facilities are subject to inspections like those of all other medicines. Pharmaceutical companies manufacturing biosimilars are required to demonstrate through comprehensive comparability studies with the reference biologic that the biosimilar is highly similar to the originator and there are no clinically meaningful differences in terms of safety, quality and efficacy.

EMA approves biosimilars according to the same standards of pharmaceutical quality, safety and efficacy that apply to all biologics. This means that when a biosimilar is approved in the EU, it has demonstrated comparable safety, quality and efficacy to the available biological reference medicine.

6. Why aren't all studies with the reference medicine repeated with the biosimilar medicine?

The effectiveness and safety of the reference biologic has already been demonstrated and established prior to the manufacturing of a biosimilar. Since the biosimilar medicine has a highly similar structure and biological activity to that of the reference biologic, not all clinical studies need to be repeated. Instead, the studies used to validate the biosimilar aim to show that there are no clinically meaningful differences between the biosimilar and the reference medicine; in other words, they aim to demonstrate biosimilarity.

7. What is extrapolation? And why can biosimilars be approved for indications for which no clinical studies have been done?

A biologic is likely to undergo some changes during its life cycle, which may be the result of changes in the manufacturing process or the administration method, for example from an intravenous to a subcutaneous delivery. A rigorous controlled process examines the changes between the initial and the "revised" biologic and the manufacturer may need to produce additional clinical data for the revised product. However, these data are usually produced in one indication only and extrapolated for all previously approved indications. Extrapolation is an established principle that applies when such major changes take place and refers to a tightly controlled process that allows a medicine to be used in additional clinical indications without the need of conducting additional clinical trials specific to each indication. By definition, a biosimilar approved by EMA matches the originator in all critical quality attributes; hence, the same extrapolation principles and concepts are applied to biosimilars. In the context of a biosimilar, extrapolation is from the originator molecule to the biosimilar molecule, based on the analytical and functional

sameness of the molecules. It is not extending the biosimilar data generated in one indication to other indications.

8. Are biosimilars as safe and effective as the original biologics?

Like any medicine approved in the EU, biosimilars can be expected to be safe and effective treatment options when they are used appropriately in their approved indications and are as safe and effective as the originators.

Instructions for their use are provided in the prescribing information (for doctors and other healthcare professionals) and package leaflet (for patients).

9. If I am already on a biologic medicine, can I be switched to a biosimilar?

It is possible to switch from a reference medicine to a biosimilar, and this is a growing practice in some countries. Any decision on switching should be made by the doctor after discussing it with the patient and taking into account any national policies regarding the use of biologics. The patient should always address with his/her healthcare team any questions related to switching from one biologic to another.

10. What should I do if I believe I have a side effect?

If you believe that you have a side effect, you should discuss it with your doctor and/or your pharmacist. It is important to report any side effect to your doctor and s/he will examine if the benefits of your treatment outweigh that of the side effect. In addition, any side effects should be reported to the prescriber either by the patient, the doctor or the pharmacist. This is a common practice for all medicines and helps authorities to continuously monitor medicine safety in the wider population. More information on how to report a side effect can be found **HERE**.