European Commission

What I need to know about

# Biosimilar Medicines

## Information for patients

*A Consensus Information Document*

Growth

This consensus information on biosimilar medicinal products was drafted by and for patients together with representatives of the European Medicines Agency, the European Commission and their stakeholders [the European Patients Forum (EPF), the European Federation of Crohn's & Ulcerative Colitis Associations (EFCCA), the Standing Committee of European Doctors, European Federation of Pharmaceutical Industries and Associations (EFPIA), European Association for Bio-industries (EuropaBio) and Medicines for Europe]. The European Commission thanks Emma Woodford (independent consultant) for the editorial and co-ordination work.

# Biosimilar medicines explained

*What do I need to know?*

This leaflet has been written for patients who want information on biosimilar medicines.[1] It aims to provide answers to some questions patients may have on biosimilar medicines. If you would like to read more about biosimilar medicines, there are references for further information at the end of this leaflet.

## *What is a biological medicine?*

People normally think of medicines being made with chemicals. However, **biological medicines** (including biosimilar medicines) come from living organisms, such as living cells that have been modified using biotechnology. This allows these living organisms or cells to produce the active substance of the biological medicine. This active substance is then harvested from the cells. These active substances (e.g. proteins) are usually larger and more complex than those of non-biological medicines.

Since the 1980's biological medicines have been developed for a wide range of conditions. Biological medicines available include hormones such as insulin and growth hormone, as well as monoclonal antibodies for the treatment of autoimmune diseases and cancers.

## *What is a biosimilar medicine?*

A **biosimilar medicine** is developed to be highly similar to an existing biological medicine. This existing biological medicine is a medicine that has already been approved and is used in the EU and referred to as the reference medicine. After the reference medicine comes off patent and finishes its exclusivity term, the biosimilar medicine is allowed to come onto the market.

Highly similar means that the biosimilar and its reference medicine are essentially the same, though there may be minor differences in their active substances. These minor differences are due to the fact that these active substances are usually large and complex molecules and that they are made by living cells.

Some degree of variability is inherent to all biological medicines and minor differences may occur among different batches of the same biological medicine. Differences may also be observed following changes in the manufacturing process of a biological medicine. Such changes are carefully regulated by the European Medicines Agency. Any differences between the biosimilar and its reference medicine are kept within strict limits to ensure that both work in the same way.

The biosimilar and its reference medicine can be compared to leaves on a tree: they appear the same and serve the same purpose, but under the microscope, there will be a very small degree of difference due to the fact they are based on biological processes. However, biosimilar medicines go through an intensive scientific assessment before marketing to ensure that, despite these small differences, they can be expected to be as safe and effective as the reference medicine.

[1] This leaflet is an update of the "Q&A for patients" which has been published 2013 as part of the consensus information document "What you need to know about biosimilar medicinal products" (http://ec.europa.eu/DocsRoom/documents/8242/attachments/1/translations)

## *Are biosimilar medicines generic medicines of biological medicines?*

Biosimilar medicines are not the same as generic medicines (a medicine which contains exactly the same molecule as an existing non-biological medicine, such as aspirin). This is because unlike non-biological medicines, biological medicines cannot be exactly copied (see explanation above).

Biosimilar medicines also have nothing to do with complementary or natural medicines nor with herbal medicines.

## *Why have biosimilar medicines been developed and approved?*

Biological medicines are treatments that can help patients with serious diseases such as cancer and inflammatory diseases. However, they are complex and can be very expensive and time consuming to develop. This can limit patients' access to such medicines, and can make it difficult for the healthcare system to afford them. Biosimilar medicines can improve patient access to such treatments and are expected to be less costly for EU healthcare systems. This is for two main reasons:

- the development of biosimilar medicines builds on the scientific knowledge obtained with the reference medicine. This means that not all the clinical studies carried out with the reference medicine need to be repeated.
- when they are introduced to the market, they need to compete with the reference medicine. This normally means that biosimilar medicines will be offered at a lower price.

However, biosimilars are not simply 'cheap copies' of reference medicines. Biosimilars are manufactured following strict quality requirements, using state-of-the-art methods, and manufacturing facilities are subject to inspections like those of all other medicines. Biosimilar medicines have been used safely in the EU since 2006 as an alternative to reference medicines.

## *How are biosimilar medicines developed and approved in the EU?*

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The European Medicines Agency (EMA) evaluates biological medicines produced using biotechnology including biosimilar medicines, before they can be approved and marketed in the EU.

The authorisation of biosimilar medicines in the EU requires a different set of data compared to other biological medicines. However, the same high standards of quality, safety and efficacy are applied.

As for any medicine, the benefits of a biosimilar medicine have to be shown to outweigh its risks before it is approved for marketing. This requires large amounts of data, including data on its purity and manufacture, how well the biosimilar medicine works and extensive comparison with the reference medicine. The comparisons are carried out in a step-wise fashion that begins with detailed studies in the laboratory comparing the structure with the function of the medicines, then moves on to comparative clinical studies (studies in humans) as necessary. Following positive assessment by EMA, biosimilar medicines are approved by the European Commission for use in EU patients.

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

Because the safety and effectiveness of the reference medicine are already well known, if the biosimilar medicine is very similar in structure and has the same biological activity, not all clinical studies need to be repeated. Instead, studies aim to show that there are no clinically meaningful differences between the biosimilar and the reference medicine (i.e. to demonstrate biosimilarity).

## *Why can biosimilar medicines be approved for indications for which no clinical studies have been done? What is 'extrapolation'?*

Because of the way biosimilar medicines are developed (see above), it is not always necessary to carry out clinical studies with the biosimilar medicine in all the conditions for which the reference medicine has been shown to work. Instead, it may be possible to extend safety and efficacy data from studies in one condition to cover others. This is known as **extrapolation**. The decision on whether to require new clinical studies for treating the other conditions is taken on a case-by-case basis by the European Medicines Agency (EMA) based on scientific evidence.

## *Who decides on the availability of biosimilar medicines in particular countries?*

Once EMA has carried out a thorough scientific assessment of their quality, effectiveness and safety, biosimilar medicines can be approved for marketing throughout the EU by the European Commission. Their availability afterwards depends on the decision by the company to place the medicines on the market together with each EU country's medicines authority and healthcare services.


## *My healthcare provider and I are thinking about choosing a biosimilar medicine for my treatment: is it going to be safe and effective?*

Like any medicine approved in the EU, biosimilar medicines can be expected to be safe and effective treatment options when they are used appropriately in their approved indications. Instructions for use are provided in the prescribing information (for doctors and other healthcare professionals) and package leaflet (for patients).

As with any treatment, it is important to have a thorough conversation with your prescribing doctor about all the available therapeutic options, their safety, benefits and risks, and the differences between the medicines, before coming to a decision.

## *If I am already being treated with a biological (reference) medicine, can I be switched to its biosimilar?*

It is possible to switch from a biological reference medicine to a biosimilar medicine and this is a growing practice in some Member States. Any decision on switching should be taken by your doctor in consultation with you, and taking into account any policies that your country might have regarding the use of biological medicines.

For questions related to switching from one biological medicine to another, patients should speak to their doctor, pharmacist or specialist nurse.

## *Getting information about treatment and use of biosimilar medicines*

As a patient to be treated with a biological medicine, it is important that you:

- Are fully informed about what can be expected when starting treatment with a biological medicine or when switching from one biological medicine to another, which could be a biosimilar medicine;
- Receive from your doctor/pharmacist all the information you need about the medicine. As with all biological medicines, a record of what medicine you have been given should be kept.
- Be a part of the decision about your course of treatment.

Like any medicines, biological medicines, including biosimilar medicines, need to be used appropriately. Patients may have different questions about how their medicine is given, and whether there are precautions or restrictions they need to bear in mind during treatment.

The answers to these questions will depend on the particular medicine you have been prescribed and on your health and medical condition.

Before starting treatment with your biosimilar medicine read the patient information leaflet that comes with your medicine, which contains important information on how to use your medicine. To ensure that patients understand which medicine they are being prescribed, especially if being switched from an originator to a biosimilar product, it is important for patients to understand that regulatory bodies have all recommended that all biologic medicines including biosimilar medicines are prescribed by brand name and not their generic name. This recommendation has been endorsed by patient and health professional organisations across Europe. If you have any unanswered questions or uncertainties about your treatment, you should speak to your doctor or your pharmacist to make sure you have all the information you need.

## *What should I do if I suspect I have a side effect?*

As for any other medicine, in cases where you suspect you may have a side effect, both you and your doctor or pharmacist should report it. This helps authorities to continuously monitor the safety of medicines in the wider population. More information can be found on the website of the European Medicines Agency.

At the time of writing this document, no specific biosimilar related safety issues have been identified for the currently approved biosimilar medicines.

## *Your Role as the Patient*

It is important that you report any suspected side effect to the prescriber, just as you would for any medicine. You should also tell your doctor if you think the medicine is not having any effect. Side effects can sometimes appear a long time after a person has been taking a medicine, or even after stopping it. Reporting your symptoms to your doctor may not only help to make you better faster, but also helps in the continuing assessment of the quality and safety of medicines.

It is also possible for you to report your symptoms directly to your national medicines authorisation body. Your doctor or pharmacist should be able to provide you with details about how to do this. Or alternatively see the reference at the end of this paper, "More information on reporting side-effects."

## *Your Doctor's or Pharmacist's Role*

In order to report suspected side-effects, your healthcare professional has to identify the medicine correctly, and document the brand name of the medicine prescribed in your patient file. They should then report the case to the relevant authorities who will use the data to check if the effect is due to the medicine and what actions need to be taken. It is important that the healthcare professional reports side effects of biosimilar medicines even if they are the same as the effects seen with the reference medicine.

## *For more information on your biosimilar medicine*

If you have been prescribed a biosimilar medicine and want more information about your individual medicine, you can get further information on EMA's website. This will take you to a page where you can access information such as the prescribing information and package leaflet (under the 'Product Information' tab) or a summary on why this medicine is approved (under the tab 'About').

## *Which biosimilar medicines are approved in the EU?*

This ***link*** lists all the biosimilar medicines currently approved in the European Union. It will be kept updated as new biosimilar medicines are approved.

## *Additional Sources of Information*

The information in this leaflet is based on a consensus document agreed by the project group Market Access and Uptake of Biosimilars and adopted by the Steering Group of the Process for Corporate Responsibility in the Field of Pharmaceuticals. The full version of the consensus information paper is available here.

## European Medicines Agency on:

Biosimilars

Medicines Safety Monitoring

Reporting side effects

## *Further information is available on the websites of these patient organisations:*

European Patient's Forum

International Alliance of Patient's Organisation

National Rheumatoid Arthritis Society (UK)

Danish Organisation for Crohn's and Colitis

Crohns and Colitis (UK)

Deutsche Morbus Crohn / Colitis ulcerosa Vereinigung

EULAR Directory of PARE Organisations

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