What do I need to know about BIOSIMILAR MEDICINES?

This leaflet has been written for patients who want information on biosimilar medicines. It aims to provide answers to some questions patients may have on biosimilar medicines.

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Q1. 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 (the substance responsible for producing the therapeutic effect) is then harvested from the cells. These active substances (e.g. proteins) are usually larger and more complex than those of non-biological medicines (e.g. paracetamol or aspirin). This complexity as well as the production methods used, means there is a natural variability in the molecules of the active substance as no two batches of biological medicine will be identical. Since the 1980's biological medicines have been developed for a wide range of conditions. Biological medicines currently available include hormones such as insulin for the treatment of diabetes and growth hormone, as well as monoclonal antibodies for the treatment of autoimmune diseases and cancers.

Q2. 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. 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.

A biosimilar medicine can only be made available on the marketplace several years after the approval of the reference medicine. This is because the reference medicine benefits from a period of exclusivity, during which biosimilar versions cannot be marketed. Therefore biosimilar medicines will only be available for use when market exclusivity has expired for the reference medicine.

Biosimilars must be thoroughly studied in clinical trials for many years to ensure they have comparable effectiveness, quality, and safety to the biological medicines they are based on. 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 there is no impact on quality, safety and effectiveness.

Q3. Are biosimilar medicines generic medicines of biological medicines?

No. A biosimilar medicine is different from a generic medicine. The term generic medicine applies to chemical (non-biological) medicines e.g. aspirin and paracetamol. The active substance in a generic medicine is an exact copy of the active substance in its reference medicine. It may not be possible to make an exact copy of the active substance in a reference biological medicine owing to its complexity, natural variability and production methods.

Q4. How are biosimilar medicines approved for use?

In Ireland, biosimilar medicines are approved by the European Medicines Agency (EMA) or the Health Products Regulatory Authority (HPRA). During the approval process the biosimilar medicine is compared to its reference medicine to show that there are no clinically significant differences between them. Regulators apply stringent criteria in their evaluation of studies comparing the quality, safety and effectiveness of the new biosimilar medicine with the reference medicine.

As for any medicine, the benefits of a biosimilar medicine have to be shown to outweigh its risks before it is approved for marketing. The studies on quality include a comprehensive comparison of the structure and biological activity of the active substances. The studies on safety and effectiveness are conducted in a specific disease setting(s) to show that there are no significant differences in the benefits and risks of the two medicines, including the risk of immune reactions (e.g. allergies). As the reference medicine has already been authorised in the EU for several years and its clinical benefit and safety is established, some studies carried out with the reference medicine may not need to be repeated with the biosimilar medicine.

A list of all biosimilar medicines approved by the EMA can be found on the EMA website. Information on whether a medicine is a biosimilar medicine can be found in the medicine's product information (under summary of product characteristics (SmPC)). Details of how the medicine was approved can also be found in the European public assessment report (EPAR). The product information and the EPAR for any medicine approved by the EMA can be found on the EMA website using the 'Find medicine' tab. Talk to your doctor, nurse specialist or pharmacist if you have any questions.

Q5. Who decides whether I receive a reference medicine or a biosimilar medicine?

Your doctor will decide this in consultation with you as the patient. If you are receiving a biological medicine for the first time you may be prescribed an original biological medicine or a biosimilar medicine if one is available.

In some cases the medicine you receive may change from a reference medicine to a biosimilar medicine or vice versa. This decision should be made by your doctor in consultation with you as the patient. Switching from a reference medicine to a biosimilar medicine or vice versa should not cause a change in treatment response. You should discuss any changes with your doctor, nurse specialist or pharmacist who will be able to answer your queries.

Q6. Can a pharmacist change the brand of biological medicine I receive?

No. Currently in Ireland a pharmacist cannot substitute a reference medicine with a biosimilar medicine or vice versa without the agreement of your doctor.

Q7. 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 have the same quality standards and be safe and effective treatment options as all other biological medicines, 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 the 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.

Q8. 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 many countries. Any decision on switching should be taken by your doctor in consultation with you, and taking into account any policies that Ireland 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.

Q9. 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) and thus 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.

Q10. 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, pharmacist or nurse should report it. You should also tell your healthcare professional 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. This helps authorities to continuously monitor the safety of medicines in the wider population.

In the case of biological medicines this report should contain the brand name and batch number of the medicine. This information ensures that the report can be traced back to the correct medicine. It is also possible for you to report your symptoms directly to your national medicines authorisation body.

Reporting forms and information can be found at HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2. Tel: +353 1 6764971 or Fax: +353 1 6762517. Website: www.hpra.ie, email: medsafety@hpra.ie.

Q11. Are there benefits to being prescribed a biosimilar medicine?

Yes. Biological medicines have revolutionised the treatment of many serious diseases such as cancer, diabetes and autoimmune conditions. However biological medicines are generally high cost and can have a significant impact on healthcare budgets. Biosimilar medicines can stimulate commercial competition which can reduce the costs associated with the use of these medicines.

As such they have the potential to generate savings and efficiencies for healthcare systems, which can help free up resources for other important aspects of healthcare without compromising on effectiveness or safety. The availability of biosimilar medicines may also increase patient access to medicines that may otherwise be unavailable to them. It's also important to know that biosimilars are not new. They have been used to treat people across Europe for over a decade.

Q12. 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, pharmacist or your nurse to make sure you have all the information you need.

Q13. What else do I need to know about the biological medicine I receive?

It is important you know the exact brand name of your medicine.
This is because biological medicines with different brand names are not identical even when the name of the active substance is the same. Any decision to change the brand of your biological medicine should be made by your doctor in consultation with you. All medicines are supplied with a package leaflet. You should read the package leaflet that comes with your medicine as it contains important information for you. If you have any questions about your medicine speak to your doctor, pharmacist or nurse.

Q14. What can my friends and family do to help?

Your family and friends can provide strong support. Communicating with each other openly and honestly about feelings and fears can help. Many people ask a friend or family member to come with them to their appointments. It can be useful to have someone else to listen, take notes and offer support. It also helps if your family understands your disease and how it is being treated. This can help everyone in the family work together to make life as good as possible for you.

Q15. Where can I get further information about biosimilar medicines?

Further information about biosimilar medicines can be found on the following websites:

Health Products Regulatory Authority (HPRA): www.hpra.ie
European Medicines Agency (EMA): www.ema.europa.eu/ema/

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Date of preparation: January 2023.

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