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**POSITION OF INNOVATIVE PHARMACEUTICAL INITIATIVE**

# ORIGINAL BIOLOGICAL MEDICINES AND BIOSIMILAR MEDICINES

about tenders and decision of substitution

*addressed to governing bodies, physicians and patients*

## Introduction [1,2,3,4]

Substitution of therapy implies the medical practice in which a physician decides to replace a product that is currently used in a patient's treatment with another product. The practice in which a physician decides to switch between different biological molecules is not new. Usually, substitution is motivated by a clinical decision to find the appropriate therapy for the patient due to inadequate efficacy and / or tolerance to the previous product.

Biological medicines, including biosimilar medicines, are medical products, commonly obtained from proteins produced by the use of living organisms. Biological medicines are generally larger and more complex than small molecule medicines, for which the clinical response depends on several factors, associated to the patient, the disease and the product, and for which the best judgment is given by the physician.

This means that:

- the physician prescribing the medicine must always retain the ability to make the decision which biological medicine should be used and the decision should primarily be based on clinical judgment, and then on the overall value of a particular medicine;
- the physician who treats a patient should, in agreement with the patient, make the decision to substitute one biological therapy with another. In cases when the substitution is performed, it must be accompanied by appropriate clinical monitoring and the patient must always be adequately informed; [1]
- bearing in mind the complexity of biosimilar medicines, substitution can lead to different treatment outcomes, as each biological medicine is unique. Due to differences in relation to a reference biological medicine, substitution for a similar medicine during treatment may theoretically stimulate certain immune responses (immunogenicity) and change in efficacy.

All biological medicines approved by regulatory bodies (e.g. European Medicines Agency - EMA) are in compliance with the latest World Health Organization's guidelines; they are safe, efficient and of high quality. Although biosimilar medicines, as the name suggests, are **very similar, but are not the same** as their original reference medicine, doctors may be encouraged within the

health system to switch the patient's treatment from the original reference medicine to some of the biosimilar medicines (or vice versa) in order to reduce costs.

This document outlines the viewpoints that are important for making the decision of substituting therapy. These viewpoints include the complexity of biological molecules, the right of patient to know the risks, achieving the best possible treatment outcomes, reducing costs with less treatment complications and circumstances under which the substitution should be considered.

The complex nature of biological molecules often used to treat patients with multiple chronic diseases means that any substitution decision should be made specifically for each case, specifically for each individual patient, disease and medicine. The approach "one size fits all" is not acceptable, but it is important that the physician aligns the level of evidence and the level of uncertainty risk in each particular case.

## The following significant risks are associated with the substitution of biological medicines/biosimilars:

- no additional clinical benefit for the patient (biosimilar medicines have similar efficacy)
- replacement may endanger the future treatment of the patient (due to exposure of already seriously ill patient to multiple biological therapies)
- adverse events that cannot be appropriately assigned and treated because of applying several biosimilar / biological medicines
- multiple cost increase in the case of adverse events, resulting from substitution, for the purpose of conducting extensive research
- the right of patients to know the risks of replacemet (an ethical question due to high risk)
- risk of medicines' substitution by the pharmacists without the knowledge and / or consent of the physician / patient (thus significantly influencing the role of the physician as the decision maker).

## When is substitution of the biological medicine not recommended?

Here are two cases in which substitution of the original reference biological medicine with a biosimilar medicine (or between medicines within a similar group) is NOT recommended:

1. **When the initial choice of treatment, such as the original reference medicine or biosimilar medicine loses effectiveness or becomes intolerable, substitution with the medicine from the same group is not recommended.** The reason for this is that all medicines within the same group have similar clinical efficacy and safety to the extent in which the substitution does not bring additional clinical benefit to the patient.

2. **If the physician considers that substitution may compromise future treatment options for the patient (e.g. with other biological therapy), substitution is not recommended,** although there is little knowledge about the consequences of multiple exposure to medicines from the same group and the immunogenicity consequences regarding future biological therapy treatment.

## Public procurement of biological medicines[5,6,7,8]

Taking into account the specific complexity of the design and implementation of public procurement for biological medicines, as emphasized by the European Biopharmaceutical Manufacturers Community, the implementation of public procurement should:

- enable effective pharmacovigilance monitoring, whereby different biological medicines (including products similar to biologicals) should be identified through a single protected product tradename
- include multiple criteria for selection (including services, devices, excellence in production, CLINICAL EXPERIENCE), not only price (based on the medicine / therapy being considered and adjusted over time)
- to provide a wide variety of products (e.g. instead of a single product, the variety of biological medical products should be available to patients) - TENDER WITH MULTIPLE WINNERS
- include an independent scientific committee in the decision-making process (ideal case involves the participation of physicians and patients with extension to pharmacists), and respect and protect the autonomy of clinical selection
- to allow the continuation of treatment (e.g. medicine substitution decision remains the clinical decision of the physician treating the patient) and to identify whether the medicine is still patent-protected in order to make note for future innovations in new therapies.

Contracting entities (which conclude contracts) must take into account Article 284 (paragraph 6) of the Public Procurement Act which states that: "If the price of certain goods or remuneration for certain services is prescribed by law or other regulation, the public contracting authority shall not in the public procurement procedure, use the price as the criterion for the selection of the tender." because the prices of medicines in Croatia are regulated by the *Ordinance on standards and the method for determining wholesale prices and the manner of reporting wholesale prices.* Also, in accordance with Article 192 of the Medicinal Products Act: "Physical and legal persons having a medicines wholesale marketing authorization are obliged to sell medicines from the basic and supplementary list of medicines of the Institute at prices determined in accordance with the Ordinance on standards and the method for determining wholesale prices and the manner of reporting wholesale prices."

**To conclude, in the procurement process, with regard to the Public Procurement Act, the decision on a tender winner may be based solely on the offered value according to defined quality criteria and not on the price of a particular medicine.**

## Conclusion

Biosimilar medicines can create room for innovation in the patient treatment and support the sustainability of the health system. Great social evolution (aging of society, chronic illness) increases pressure on the health system's sustainability in Croatia, but also throughout Europe.

The use of biosimilar medicines could generate, along with other procedural measures, savings which would then enable further financial investment in finding innovative medicines. Such policy should be implemented in the light of the principles that should always be taken into account in the development and implementation of procedural measures such as the continuity of patient's treatment and the role of physicians as decision-makers.

The physician is the key person to evaluate the patient, the disease and the medicine when deciding whether or not to replace the biological medicine that the patient is receiving at that moment with another biosimilar medicine. For this reason, the physician should remain independent in making decisions and have an unlimited choice of prescription medicines. The physician should assess the level of risk in biological therapy substitution in each particular case and associated uncertainties during the substitution, as well as the availability of evidence regarding safety of such substitution. When physicians think about the therapy substitution, it is important to take into account the history of the patient's disease and to carefully record the substitution in the patient documentation, as well as the protected name and serial number of prescribed and applied medication.

Also, when considering substitution, physicians should be well-informed about the medicine and in an understandable and acceptable way fully inform the patient, while healthcare workers (physicians, nurses, pharmacists) should carefully monitor changes and record any adverse events.

An effective pharmacovigilance system (PV) of biological medicines is important, especially when several treatment options are available. Tracking of medicines is crucial for biological medicines, even more than for other medicines, because of potential immunogenic effects, through the prescribing cycle, application, recording and reporting about biological medicines. In order to achieve this, medicines identification measures under a protected name and serial number are also required in regulations and in practice. Yet, much of this effort lies on an

efficient PV system and on safe reporting practices not only of regulatory bodies, but also of health professionals, patients and the general public.


Croatian association of innovative medicines manufacturers iF! (Innovative Pharmaceutical Initiative) has been gathering and representing 23 innovative pharmaceutical companies employing 812 employees and providing nearly 60% of medicines in Croatia for 23 years. The association is a member of EFPIA - the European Association of Innovative Pharmaceutical Companies and Associations based in Brussels. More detailed information can be found at www.ifi.hr.

*iF! members:*

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## LITERATURE

1. EBE, EFPIA, IFPMA; Considerations for physicians on switching decisions regarding biosimilars, March, 2017
http://www.efpia.eu/mediaroom/384/43/EBE-EFPIA-and-IFPMA-have-today-launched-a-position-paper-entitled-Considerations-for-physicians-on-switching-decisions-regarding-biosimilars

2. American Chamber of Commerce in Croatia; Using Public Procurement to Improve Healthcare Services in Croatia, April 2016
http://www.amcham.hr/pages/menuId:53/pageId:68

3. French Biosimilar Law – No generics-style substitution policy
http://www.ebe-biopharma.eu/

4. European Commission: What you Need to Know about Biosimilar Medicinal Products, Consensus Information Paper 2013.
http://www.medicinesforeurope.com/2015/02/22/test-article-p/

5. Public Procurement Act, OG 120/2016, Article 284

6. Medicinal Products Act, OG 76/2013, Article 192

7. Bylaw on the criteria and mode for determining of medicines prices and reporting.

8. Position of Innovative Pharmaceutical Initiative: Why Medicines are not Subject to the Public Procurement Act, 2017