Position paper of the Finnish Society for Rheumatology on biosimilars

Biosimilars

A biosimilar is a generic pharmaceutical product similar to an originator biologic product which has lost its patent protection and which has been approved and granted marketing authorization by the European Medicines Agency (EMA).

When approving a biosimilar, the EMA requires that comprehensive comparisons of the physicochemical structure of the biosimilar and the originator biologic product have been carried out and that the biosimilar has thus been found to be similar to the originator biologic product and that at least one randomized clinical drug trial has been carried out where the safety and effect as well as the pharmacokinetics and pharmacodynamics of the biosimilar has been found to be similar to the originator biologic product.

Loss of patent protection and loss of right to exclusivity are organic phases of the life span of original medicinal products. The use of biosimilars allows price competition and price reductions. This implies that more patients may be treated at the same cost and that new drugs can be granted reimbursement. Price reductions of biologics also opens the economical possibilities for developing countries to increase the use of biologic products for treatment of illnesses.

Most biosimilars used to treat rheumatological illnesses are administered by the patient himself/herself injecting the product subcutaneously with an injector, the use of which varies among the products. The patient is instructed thoroughly in how the biologic introduced for his/her treatment is to be administered. This is usually done within the specialized health care system. If a biologic product is changed into another biologic product, care must be taken that the patient is able to use the injector of the new product properly. Changing biologics in this way is done best and safest under the supervision of a health care unit.

Recommendation for selection of biologic

According to the evaluation of the Finnish Society for Rheumatology (FSR) significant societal savings are possible if the market of biologics develops. This should be taken into consideration A) when treatment with any biologic is introduced and B) when the continuation of treatments started earlier is considered.

A) Selecting the first biologic for a patient: The FSR recommends consideration of the cost-effectivity of biologics in three stages:

1) Selection among product groups (e.g., TNF-α blockers, IL-6 inhibitors, CD20 antibody, CTLA-4-Ig, IL-1 inhibitors, IL-17A inhibitors, IL-12/23 inhibitor) requires therapeutic considerations. If groups are considered therapeutically equivalent, the FSR recommends choosing the most cost-effective therapeutic group that has undergone price competition.

2) Regarding the selection of a product within a therapeutic group (e.g., TNF-α inhibitors), the FSR recommends primarily the most cost-effective biologic that has undergone price competition, unless therapeutic circumstances (e.g., comorbidity, pregnancy, lactation or incompatible dosing practices) favor the choice of another product.

3) The final choice of biologic (product name) should be the most cost-effective product available.

B) The FSR recommends that previously started biologics are discontinued and replaced by the most cost-effective pharmaceutical product, if there is a significant price difference between the product used by the patient and the most economical product available (example: an original product could be switched to a corresponding biosimilar).

The National rheumatologic coordination center (Tays Central Hospital , Pirkanmaa Hospital District) maintains a scoreboard comparing the prices of biologics in Finland.

Special circumstances to consider regarding use of biologics in rheumatology

1. **Biologics are resorted to** in rheumatology only if the inflammatory activity of the rheumatic disease has not abated on traditional pharmaceuticals used in rheumatology or if such drugs are inappropriate for the patient.

2. **Before staring a biologic** (original product or biosimilar), a specialist physician proficient in the use of biologics must make an assessment of the expected benefits and drawbacks of the biologic intended for use with consideration of the specific patient being treated. This consideration includes patient age, comorbid illnesses, medication, previous illnesses, special consideration of the patient's risk of infections and the patent's current functional ability.

3. **At the start of a biologic** (original product or biosimilar) the required preliminary tests must be carried out to guarantee drug safety.

4. **Switching between original product and biosimilar** should be decided by the responsible specialist and after the patient has been informed in detail. Switching to another product is possible only after the patient has used the product for a sufficient period of time (minimum 3 months) during which the effect and tolerability of the biologic has become established.

   The use of biosimilars could be promoted by an information campaign to the public describing the benefits of biosimilars. This would improve patient compliance when switching to biosimilars. The same goal is maintained at the meetings of the Finnish Society for Rheumatology, where the use of biosimilars is also promoted.

5. **The FSR does not currently consider prescription switching at pharmacies as the primary measure** to promote the use of biosimilars. Costwise, the increased use of biosimilars, if switching at pharmacies would be allowed, would, in fact, increase expenditures because of the increased costs related to instructing patients the use of injectors and an increased number of visits to health care services. Prescription switching at pharmacies might also impair treatment compliance and treatment effectiveness experienced by patients and increase the occurrence of adverse event experiences of patients.

6. **Immunogenicity of biologics.** All biologics may generate antibodies, which cause loss of drug effect. The FSR recommends assessment of residual drug concentrations and drug antibody titers of original biologics and of their corresponding biosimilars, if needed. This applies especially for patients whose treatment response is lost. Randomized switch studies involving a single switch did not disclose any problems of drug effect nor safety. Because there is, thus far, a lack of data on the immunogenicity of repeated switches, the FSR recommends that the effect and safety of biosimilars and their corresponding original products and the safety of switching from original to biosimilar and/or back should be followed up by recording data in a national rheumatological register.

7. **Biosimilars in the treatment of pediatric rheumatological diseases and rheumatic ocular inflammations.** There are only a few suitable pharmaceutical products (dosage and device for administration) for children and biosimilars are not universally available. There are not many effective pharmaceuticals to treat severe pediatric eye inflammations (uveitis/iritis), primarily TNF-α inhibitors are used. It is important that there are no discontinuations nor compliance issues in drug treatment, since these phenomena increase the risk for anti-drug antibodies and thus for loss of drug effect. Familiarizing the entire family (child and parents) with the correct use of drugs and injection technique must remain the responsibility of a health care unit specialized in pediatric rheumatology.

8. **A national register covering all patients taking biologics** would provide a better guarantee for safety control, facilitate the follow-up of effectivity and adverse events of biologics and promote the assessment of scientific research and cost-effect assessments in this field of medicine. Authorities responsible for drug safety and consortia (e.g., hospital districts) responsible for patient treatment are urged to participate in covering the costs for maintaining this registry.

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