

ABSTRACTED SCIENTIFIC CONTENT

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Essential information for internists on biologicals and biosimilars

Authors from the IRCCS – *Istituto di Ricerche Farmacologiche 'Mario Negri'*, Milan, Italy discuss some of the most frequent concerns raised by internists (doctors of internal medicine) about biosimilars [1]. They also try to explain the scientific principles underlying the biosimilar concept established in Europe that allows for the licensing of biosimilars in the European Union.

While the demonstration of bioequivalence is sufficient for small molecule generic drugs, this approach is not scientifically applicable to biosimilars. Generics must demonstrate that the active ingredient of the generic drug is the same as that of the originator drug. Therefore, internists and patients can expect that generics will have the same properties, the same efficacy, and the same safety characteristics as the originator product.

In contrast, biologicals are usually large, complex molecular structures derived from or produced in living organisms, making them very difficult to replicate. Even for the originator biological, small changes in the manufacturing process can cause changes in the final product, making things even more complicated for potential biosimilars. Therefore, biosimilars of such molecules can only be similar, but not identical, to the originator and are also subject to different related post-translational processes. This is of concern for physicians, who worry that if a reference product and its biosimilar are not structurally identical they might not be therapeutically equivalent.

The development process for a biosimilar ensures a comparable risk-to-benefit balance compared with the originator biological. Thus, based on an extensive developmental programme there is no scientific reason to consider that a biosimilar would be different from the originator when used in clinical practice according to the approved indication. Moreover, according to the available evidence and pharmacovigilance network, there are no grounds to believe that the use of a biosimilar carries more risk for the patient than the use of an originator biological. Internists should be also reassured with regard to immunogenicity and safety issues. It is well known that the problem of epoetin antibody-induced pure red cell aplasia (PRCA) was first recognized after the formulation of the originator epoetin Eprex (epoetin alfa) was changed [2].

Furthermore, there is a need for the dissemination of clear information about existing guidelines, access to unbiased information and educational interventions regarding the clinical utility of biosimilars. The aim of this should be to help internists to improve their knowledge and to implement the use of these medications in clinical practice. In Europe, there is a clear gap between the regulatory decisions that govern biosimilar approval and the recommendations of medical societies. The fact that the views of medical societies, whose members are the physicians that will prescribe biosimilars, disagree with those of regulators, may hold back biosimilar uptake [3].

The need for the benefits of biosimilars to be communicated has also been highlighted at a biosimilars roundtable organized by GaBi (Generics and Biosimilars Initiative) in Brussels, Belgium on 12 January 2016. Representatives of medical societies attending the biosimilars roundtable concluded that, while the European Medicines Agency (EMA) has carried out important work looking

at extrapolation and investigating the safety of biosimilars, their findings have not been communicated effectively [4, 5].

One of the main expected benefits of the introduction of biosimilars is a reduction in costs and as a consequence to extend the access to new innovative biotherapeutic drugs. Despite this aim, the scientific principles used for defining comparability are the same as those applied to an already approved originator biological after a significant change in its manufacturing process. Starting from this evidence, internists should only prescribe medicines for which the quality, safety and efficacy have been demonstrated according to state-of-the-art science and technology, irrespective of whether they are originator biologicals or biosimilars.

The future development of biosimilars will depend on the definition of reliable parameters of interchangeability and will require further advances in knowledge on the characterization of the molecules. Internists, as well as other clinicians, along with healthcare providers and patients, will play a key role in determining how biosimilars are integrated into clinical practice.

In order to facilitate understanding, the authors also list a number of 'essential references' for internists concerned about biosimilars.

Essential references

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