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NOVELTIES IN DERMATOLOGY

Biosimilars in Dermatology: Current Situation (Part I)☆

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Abstract The first biosimilar version of a biologic agent used to treat psoriasis (infliximab) entered the Spanish market on February 16 of this year, and more biosimilars can be expected to follow in the coming months and years. Logically, this new situation will have economic repercussions and alter prescribing patterns among dermatologists. In this article, we review regulatory issues related to the approval of biosimilars, with a particular focus on the situation in the European Union. We will examine analytical characterization studies and special considerations for clinical trials with biosimilars, and also look at several somewhat contentious issues, such as the extrapolation of indications, interchangeability, and automatic substitution. Finally, we will review the biosimilars with indications for psoriasis currently in the clinical development pipeline and assess their potential to offer comparable efficacy and safety to the reference product while contributing to the sustainability of the public health care system.

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Biosimilares en dermatología. Situación actual (parte I)

Resumen El 16 de febrero de este año se han comercializado en España los primeros biosimilares de un tratamiento biológico para la psoriasis (infliximab), y en los próximos meses y años está prevista la incorporación de otros biosimilares, con un previsible impacto económico y en los hábitos de prescripción dermatológicos. En la presente revisión se abordan los aspectos regulatorios de la aprobación de biosimilares, con especial referencia al entorno de la Unión Europea, prestando especial atención a la caracterización analítica de la biosimilaridad y las consideraciones especiales referidas al diseño de ensayos clínicos con biosimilares. También se abordan aspectos objeto de cierta controversia, como la extrapolación de indicaciones, la intercambiabilidad y sustitución automática, los biosimilares en fase clínica de desarrollo con indicaciones que incluyen la psoriasis y unas consideraciones finales sobre el potencial de estos fármacos para proporcionar unas alternativas terapéuticas de eficacia y seguridad comparables a las de sus productos de referencia, contribuyendo a la sostenibilidad del sistema sanitario público.

Introduction

The development of biologic agents in recent decades has substantially improved outcomes in the treatment of psoriasis and psoriatic arthritis, as well as other chronic inflammatory conditions. Drugs such as anti-tumor necrosis factor [TNF] agents and anti-interleukin 12/23 agents have now become available as safe and effective alternatives. However, the elevated cost of their production and marketing, coupled with the fact that some of them have lost or will soon lose patent protection, and the technical feasibility of producing new biosimilar drugs, has prompted an interesting debate with repercussions in medical, social, and public health sectors. The possibility of extending coverage of this type of therapy to a greater number of patients and reducing production costs is one of the most attractive aspects of the arrival of the so-called biosimilars. The health authorities, supported by scientific evidence, need to guarantee that these products are equivalent to their reference biologics in terms of safety, efficacy, traceability, and pharmacovigilance. The present review covers technical aspects of biosimilars as well as the controversies that their arrival is generating in dermatology.

A biologic agent is a drug that contains one or more active substances synthesized or derived from a biological source. Given the complexity of these molecules and the possible variations in their production process, a certain degree of variability is present, even within different batches of the same drug. The European Medicines Agency (EMA) defines biosimilars as ''a biological medicine that is developed to be similar to an existing biological medicine (the 'reference medicine')."[1]

The European Union (EU) was the first region to define a legal and regulatory framework for biosimilar drugs (more often referred to simply as biosimilars). The EU lead has been followed by several other countries, such as Australia, Canada, Japan, and the United States, and also organizations such as the World Health Organization (WHO). The first biosimilar was approved by the European Commission in 2006. In the EU, marketing authorization applications for drugs derived from biotechnology methods (including biosimilars) must be evaluated by the EMA through a centralized procedure. The European Commission then authorizes these drugs on the basis of the scientific opinions issued by the EMA. The resulting marketing authorization is valid in all EU member states. For a biosimilar to be authorized, the applicant must have demonstrated that the differences between the biosimilar and the reference medicine do not significantly impact safety or efficacy, and the biosimilar can only be launched once the patent for the reference medicine has expired.

Biosimilars and Generics

Biologics are obtained from living systems and their exact characteristics and properties depend to a large extent on the manufacturing process. Biosimilars must meet a series of strict requirements in terms of analytic characterization, pharmacokinetic, and pharmacodynamic similarities, as well as efficacy and safety equivalence with respect to the reference product. In contrast, generics are bioequivalent copies with the same active substance, same dose, same pharmaceutical form, same route of administration, and very similar bioavailability. Such products are manufactured using readily reproducible chemical processes. Trials to test therapeutic equivalence are not required prior to approval. Both biosimilars and generics are cheaper than their proprietary counterparts, but biosimilars are normally more complex and expensive to produce, characterize analytically, and develop than generics.[2] The clinical development program for a biosimilar is cheaper than the original biologic but the pharmacovigilance burden is similar.

Biosimilars are authorized by the competent authorities according to demonstrated comparability with the reference product. The clinical database is limited and often only includes data related to the main indication (or to one of the indications). Biosimilar manufacturers are required