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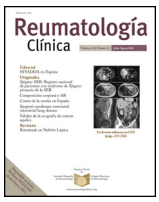

Special Article

Current State of Biosimilars in Mexico: The Position of the Mexican College of Rheumatology, 2016☆

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ABSTRACT

The present document is a position statement of the Mexican College of Rheumatology on the use of biosimilars in rheumatic diseases. This position considers that biosimilars should be considered as interchangeable, that automatic substitution without previous notice in stable patients during follow-up is not ethical, that the approval of a biosimilar should only be given after exhaustive review of preclinical and clinical data marked by Mexican regulations, that it should be clearly stated in the nomenclature of biologic drugs which is the innovator and which is the biosimilar, that it is not correct to choose a biosimilar as treatment based only on economic reasons or extrapolate indications based only on the approval of the innovator and in the absence of safety and efficacy data for the biosimilar.

Escenario actual de los medicamentos biocomparables en México: posicionamiento del Colegio Mexicano de Reumatología, 2016

Palabras clave:
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RESUMEN

El presente documento refleja el posicionamiento del Colegio Mexicano de Reumatología y de expertos sobre el uso de medicamentos biocomparables (conocidos como biosimilares en otros países) en enfermedades reumáticas. En resumen, este posicionamiento considera que si bien los biocomparables deben considerarse como intercambiables, no es ética la sustitución automática de medicamentos sin previo aviso en pacientes estables durante el seguimiento; que la aprobación de un biocomparable debe llevarse a cabo solo después de revisar exhaustivamente las pruebas preclínicas y clínicas señaladas por la ley mexicana; que debe modificarse la

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forma de enfatizar en su nomenclatura que se trata de un medicamento biotecnológico innovador o biocomparable de manera clara; que no es adecuado elegir como tratamiento un biocomparable basándose únicamente en aspectos económicos ni realizarse la extrapolación de indicaciones basándose únicamente en la aprobación obtenida por el innovador y en ausencia de datos de seguridad y eficacia para el biocomparable.

Introduction

The introduction of biological drugs has produced a watershed in the history of the treatment of chronic disabling, and even potentially fatal, diseases, as occurs in oncology, where biological agents, in particular cases, are less toxic and lead to longer survival than conventional treatments; with respect to rheumatology, their success has been much more evident in diseases like rheumatoid arthritis (RA) or spondyloarthritis, in which a considerable percentage of patients achieve clinical remission, a condition that, in the past century, was attained in less than 20% of the patients.[1] In addition, it is evident that patients return to work, which represents less expense for health institutions. Currently, we are faced by the expiration of the patents of certain innovative drugs and, with this, the arrival of the so-called biosimilar drugs, which in Mexico are referred to as "biocomparables". In accordance with the established definition, a biosimilar drug is a noninnovator biological product that has been shown, by means of tests established in the Mexican regulatory framework, to be comparable to the reference biological drug in terms of safety, quality and efficacy. On the international level, these drugs are known as biosimilar medical products.[2] It is worth mentioning that biosimilar medicines are in themselves biological agents and the major difference lies in the fact that the innovators launched the product and the formulation was replicated when the patent expired.

The introduction of biosimilar drugs is accompanied by the possibility of reducing the cost of antirheumatic treatments and increasing their availability when the patents of the reference products expires, based on the supposition of their lower cost.[3] One of the current advantages of these products is that, once the comparability of a drug has been demonstrated, they may obtain approval from health agencies for the same therapeutic indications authorized for the innovator drug,[4] provided they can make available the scientific evidence that enables the extrapolation of these indications. Biosimilars can be acquired in the European Union since 2006[4] (with the approval of Omnitrope®, somatropin), in the United States since 2015 (with the approval of Zarzio®, filgrastim) and in Mexico since 2014 (with the approval of Zarzio®, filgrastim).

Currently, among the therapeutic options in rheumatic diseases, there is only one biosimilar approved for marketing in Mexico; this product, referred to as CT-P13, is an infliximab biosimilar. This was accomplished by applying the existing legislation on biosimilars. The biosimilar drug is known as Remsima®; nevertheless, a number of biosimilar drugs are now under development and soon there will be more on the market. The regulatory framework to which biosimilars are subjected has undergone changes. For example, the introduction of NOM-257-SSA1-2014 concerning questions related to biotechnological medicines. According to the most recent version, approval requires the presentation of characterization data and clinical trials involving patients, which are also included in other updated regulations and reference guidelines.[5] In rheumatology, certain biological drugs have encountered access barriers to their approval and prescription on the part of physicians, favored in part by the introduction of biological products authorized prior to the current Mexican regulatory framework. In light of new scientific evidence, the Mexican College of Rheumatology (CMR) presents an update of its position with respect to biosimilars, which was published for the first time in 2012.[6]

Definitions

In Mexico, as we mentioned above, biosimilars are defined as noninnovator products that have the characteristics of quality, efficacy and safety comparable to those of the reference drugs.[6,7] There are other so-called biotechnological medicines,[8,9] still yet to be classified, which were registered prior to the current regulatory framework for biosimilar drugs; for these cases, *Norma Oficial Mexicana* (Official Mexican Standards) NOM-257-SSA1-2014,[5] establishes those drugs that must undergo a review of the health registration process in accordance with article 157 of the Regulation on Health Supplies, for the purpose of meeting the requirements established by the General Health Law.[10]

The term "comparability" refers to the technical evaluation of the quality attributes and the impact of changes in the manufacturing process in the different stages of the biotechnological development or after approval of the product. This can involve analytical and clinical testing that demonstrate that the quality, efficacy and safety are equivalent to those of the reference product.[11–14] "Equivalence" refers to the fact that the biosimilar has a qualitative and quantitative composition comparable to that of the reference drug, provides the same therapeutic effect[15,16] and complies with a high level of comparability with the reference product approved by the authorities.[17]

Clinical safety of biosimilars is not assessed only in terms of adverse events; it also involves the evaluation of the immunogenic potential, defined as the ability of a molecule to provoke a long-term adaptive cellular or humoral immune response and generate immunological memory.[18,19] Aside from pharmacokinetics, pharmacodynamics, safety and efficacy, which are evaluated in the majority of clinical trials with biosimilars to be employed in the field of rheumatology, there are other characteristics of biosimilar drugs that should be taken into account to establish a stance on their use. Here we provide their definition.

Traceability is understood to be the ability to reconstruct the history, route or application of a drug product, thus identifying the origin of its components, the processes it undergoes and its distribution and storage from its production and throughout its entire "life cycle". It consists in being capable of identifying the stages that a product has gone through during the process of being manufactured (manipulations, composition, machinery employed, temperature to which it was subjected, batch number, etc.), which are considered important and can produce variations in the final product that reaches the consumer.[20,21]

Nomenclature

At the present time, in Mexico and other countries, innovator products and biosimilars are marketed and distributed under the same international nonproprietary name as the active ingredient. Therefore, both products share the same code assigned by the health sector. If the products are on the list of essential medicines, this administrative process, regulated by the Secretariat of Health