Biosimilar product labels in Europe: what information should they contain?

In 2016, a multi-stakeholder workshop was held on the topic of 'Biosimilar Labelling'. The discussions concerning labelling particulars are outlined in this meeting report.

Keywords: Biosimilar, labelling, patients, pharmacists, physicians, Summary of Product Characteristics (SmPC)

Introduction

Labels on medicinal products contain information for pharmacists, physicians and patients. This information is presented in the Summary of Product Characteristics (SmPC), the Patient Leaflet (PL) and the immediate label on the outer product packaging, referred to as 'labelling' in this report.

Biological medicines (biologicals) are complex molecules, often proteins, though they may contain also sugars or nucleic acids, and are manufactured in, extracted from, or semi-synthesized from biological sources. Biosimilar medicines are defined in the European Union (EU) as a biological medicinal product that contains a version of the active substance of an already authorized original biological medicinal product (reference medicinal product) in the European Economic Area [1]. Due to the similarity, yet difference, between originator biologicals and biosimilars, questions have been raised about current EU labelling practice for biosimilar medicines.

Once authorized, the European Medicines Agency (EMA) applies a 'same-label' (generic) approach to biosimilar product labels [2, 3]. This means that the information on the labelling of the biosimilar should be a copy of the approved labelling of the reference product, with the exception of the pharmaceutical particulars. Section 5.1 of the SmPC, a document not usually available to patients, will include a statement declaring that the product is a biosimilar, but this is the only part of the labelling where this information can be found. Neither PLs nor the immediate labels contain this information.

There are concerns in Europe over whether information on labels is sufficient to meet the needs of the end users, or whether amendments are necessary. The role of product labelling in building user confidence in biosimilar products is subject to discussion [4]. In the US, proposals for amendments to biosimilar product labels are already underway [5].

To discuss current labelling of biosimilars in Europe, the European Biopharmaceutical Enterprises (EBE) and the European Association for Bioindustries (EuropaBio) held a multi-stakeholder workshop on the topic of 'Biosimilar Labelling', in Brussels, Belgium on 2 February 2016. The purpose of the meeting was to gain an understanding of how stakeholders use or consult medicinal product information, and to investigate their preferences for the content of biosimilar labels. The focus of discussions was on the perspectives of the end users, namely patients, pharmacists and physicians.

Methods

A multi-stakeholder workshop on the topic of 'Biosimilar Labelling' was held in Brussels, Belgium on 2 February 2016. Of the 40 invited participants at the workshop, there were representatives from patients, physicians, pharmacist associations, academia and industry. Representatives of EMA attended the workshop by telephone as observers.

During the first part of the workshop, presentations were given by the industry to provide a basic working knowledge on the concept of biosimilarity and on medicinal product labelling in general. Subsequently, representatives from pharmacist, physician and patient organizations presented their perspectives on biosimilar labelling. The second part of the workshop was dedicated to discussions around the actual usage of SmPC and PL. Participants undertook discussions in mixed stakeholder groups, to reflect on the viewpoints of the presentations and identify the key labelling elements which could be improved.

Summary of stakeholder perspectives

An overview of the comments expressed by the various representatives of stakeholder groups is summarized below.

The pharmacists' view of biological and biosimilar labelling

Throughout their presentation and the discussion, pharmacist representatives stated that it is very important to have a clear and understandable naming system for biologicals. Having such a system in place, ideally internationally agreed, would assist in global traceability and pharmacovigilance.

Pharmacists, in particular hospital pharmacists, regularly work with the SmPCs, and frequently consult the European public assessment report (EPAR). The representatives stated that the SmPC should be fit for purpose and not become more extensive than at present. As such, it should not include more data per se, but clear cross-references to specific sections in the EPAR, e.g. section X, paragraph Y, line Z, should be available. These cross-references could then be used to explain, e.g. which data were extrapolated, or any specific pharmacovigilance requirements.

The physicians' view of biological and biosimilar labelling

The physician representatives advocated a need for more transparency in the labelling of biosimilars. They voiced that information should be more reliable, clear and easily accessible.

The representatives stated that the most important element for a physician prescribing a biosimilar is assurance that it will be as effective and safe as its reference product. As such, they stressed that any measures aimed at increasing prescription rates of biosimilars should always take safety and efficacy into account. It would be important to ensure that updated information on pharmacokinetics, immunogenicity and switching is always available to physicians. Additionally, the physician representatives thought that adding a statement to the label of a biosimilar medicine, declaring which indications were extrapolated and which indication(s) underwent clinical study could provide more clarity to prescribers. They also

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highlighted that labels should provide information to ensure product traceability.

In agreement with the perspective of pharmacist representatives, physician representatives did not want the SmPC to increase in length or complexity of information. They also thought that the addition of specific cross-references to actual data sources, such as sections in the EPAR, would be helpful with keeping the length of the labelling as is.

The patients' view of biological and biosimilar labelling

Representatives from various patient associations expressed the patients' perspective on biosimilar labelling at the workshop. Patient representatives stressed that patients have the right to know what product they are being administered, and specifically, whether they are receiving a biosimilar or an originator biological. In this respect, the idea that a biosimilar patient leaflet should include an explanation of what a biosimilar is was thoroughly discussed. In order to enable patients to report any adverse events more effectively, it was considered important for the labelling to clarify, when a medicine is a biosimilar, that the listed adverse effects relate to the originator biological and to encourage reporting also of adverse effects that are not listed. Patients should also be aware that different versions of the same biological (the originator product and different unique biosimilars) may be available and brand name reporting of adverse effects should be encouraged. All information supplied to patients should be adapted to their specific needs. As a result, labelling guidelines should take all patient requirements into account to ensure every patient is adequately informed.

Overall, patient representatives stressed that there is a need for access to clear, transparent and real-time information, designed for patients. This should include the availability of disease-specific information such as extrapolation of clinical data. However, patient representatives did not reach a conclusion on where general elements of such information should be placed, be it in the labelling or in additional educational materials.

Additional outcomes

There was discussion over the fact that patients, especially in hospital settings, are often fully dependent on their doctors when it comes to drug administration and information. They do not see the label and rely on their physician having an appropriate understanding about the product they receive. When it comes to seeking additional information, both physician and pharmacist representatives declared that they refer to the labelling during prescribing and dispensing, and so this is an important vehicle for information. However, the frequency of reference to labelling depends on the individual prescriber and the situation. Examples when reference to the labelling is commonly made include making new treatment decisions, responding to questions from patients and comparing products.

Issues outside biosimilar labelling were also discussed during the workshop, including education on biosimilarity, accessibility to biosimilar information, i.e. where to find documents; and suitability, i.e. whether the information provided is understandable to the lay reader.

Conclusions and future perspectives

This workshop on biosimilar labelling saw discussions that highlighted concerns over the quantity and quality of information available on the labelling of biosimilars in Europe. All stakeholder representatives, including pharmacists, physicians and patients, agreed that there is value in adding more information on the labelling of all biological medicines. However, all were aligned in that the length of the documents (specifically the SmPC) should not increase. Pharmacist and physician representatives also expressed that the need for additional information could be addressed through cross-references to relevant information sources, such as EPARs, enabling easy access.

All participants agreed that improving transparency was important and that labelling should be adapted to fit the needs of patients, pharmacists and physicians. During the discussion, the most important changes put forward to improve labelling transparency referred to indicating the type of product, i.e. biosimilar; extrapolated indications; cross-referencing relevant sections of the EPAR where more detailed and specific information can be retrieved.

Beyond labelling, all stakeholders agreed that there is a need for better general understanding of the concept of biosimilarity. Availability of educational material tailored to each stakeholder group would improve understanding. Increasing awareness and education would make patients and physicians more comfortable when provided with the option of a biosimilar medicine.

The workshop conclusions were in line with the results of EuropaBio's more recent survey of European physicians [6, 7]. Here, physicians indicated that they would prefer more product specific information on biosimilar labels (SmPCs).

Overall, all stakeholders agreed that biosimilar labelling in Europe can be improved although the views on how to improve labelling differed. Medicines for Europe, whilst consulted regarding their opinion, did not support the conclusions of the workshop. Open discussions involving all stakeholders including regulators need to be taken forward to develop potential changes and bring them to a point where they are implemented in product labelling.

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