Multi-stakeholder Workshop on Biosimilar Medicinal Products

A follow-up event to the Process on Corporate Responsibility in the Field of Pharmaceuticals

Brussels, 20 June 2016

Summary
Framework and objectives

While in the European Union decisions regarding pricing and reimbursement, interchangeability and prescription incentives lie within the responsibility of each Member State, the European Commission is committed to foster dialogue among a broad range of stakeholders at European level as a means to ensure a long-term sustainable development and the best access for patients to safe and high quality medicines.

Since 2010 a multi-stakeholder dialogue and co-operation at European level has been put in place under the Process on Corporate Responsibility / Access to Medicines in Europe including a Working Group on Market Access to and Uptake of Biosimilar Medicinal Products.

The multi-stakeholder workshop held on 20 June 2016 in Brussels was the second follow-up event to the activities related to biosimilar products under the Process (2010-2013).

Major societal challenges like an aging population in the EU or emerging new and old health threats but also the aftermath of the financial and economic crisis put a growing pressure on the sustainability of public healthcare budgets. EU Member States are considerably challenged with finding a balance between the need to ensure the financial stability of health and care systems and growing patients' expectations to get access to innovative and effective medicines which are often costly.

Biosimilars, biologic medicines which are highly similar to an originator biologic medicine already licensed for use, have significant potential to create competition in the market and provide more affordable access to biological medicines for the treatment of many severe diseases including cancers and autoimmune diseases.

EU looks back on a "European success story" with regard to biosimilars. The first biosimilar was approved 10 years ago and the European Medicines Agency has created a dedicated and comprehensive regulatory pathway which is recognised to be the gold standard world-wide.

Besides regulation and market approval the European Commission (Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs) has been also aiming at enhancing collaboration between all interested and concerned stakeholders (patients, physicians and other healthcare professionals, payers, the Member States' competent authorities and the pharmaceutical industry) in order to find common non-regulatory approaches for more timely, equitable access to and informed uptake of biosimilars after their Marketing Authorisation.

This so called "multi-stakeholder approach" helps to build a common understanding and trust between doctors and patients, payers and the commercial operators.

---

1 Commission Staff Working Document Pharmaceutical Industry: A Strategic Sector for the European Economy, SWD(2014) 216 final
This multi-stakeholder workshop on biosimilar medicinal products was organised in close cooperation with the European patients' and doctors' associations and the industry organisations.

The main objectives of this year's event were to:

(1) present the update on the impact of biosimilars competition;

(2) provide an opportunity for gathering all relevant interested stakeholders to facilitate an exchange of information and experiences: Based on the outcomes of the first follow-up event in October 2015, this year's workshop aimed at looking deeper into the experiences at national level including available evidence on the use and integration of biosimilars into healthcare pathways, the information and communication needs of patients and healthcare professionals, and the challenges and best practices for patient-healthcare communication in different settings;

(3) launch the updated version of the Question and Answers document on biosimilar medicinal products prepared for patients and doctors.

**Outcomes**

**Impact of biosimilar medicinal products on competition (IMS Health Report 2016)**

The first update of the report "The Impact of Biosimilar Competition" prepared by IMS Health in co-operation with the European Commission and its stakeholders and presented by Per Troein, Vice President IMS Health Strategic Partners at the workshop sees the main drivers for the biosimilar market in the loss of exclusivity of many biological blockbusters in the coming years, the already extensive pipeline of biosimilars expected to come to market and the growing pressure on the healthcare systems to increase access to biologicals.

The report sets out to describe the effects on price, volume and market share following the arrival and presence of biosimilar competition in the European Economic Area.

IMS Health has accompanied the report by five observations on the biosimilar competition in the EU:

---

2 The first report was published in 2015, see http://ec.europa.eu/docsroom/documents/14547/attachments/1/translations. The current update is based on 2015 figures: http://ec.europa.eu/growth/tools-databases/newsroom/cf/itemdetail.cfm?item_id=8854

3 EU28+EFTA (Iceland, Liechtenstein, Norway)
The rationale behind the introduction of biosimilars is to increase price competition resulting in reduced prices and increase patient access to treatment. The increased competition through biosimilars affects not only the price for the directly comparable reference product but also has an effect on the price of the whole product class. It can have a similar or even a larger impact on the total therapy area price as it has on the biosimilar/reference product price. The countries with the highest competition show reductions that achieved up to 50-70%.

The correlation between the market share of biosimilars and the price reduction is very weak, i.e. there can be a low biosimilar market share and high price reductions or the reverse. But even if the biosimilar product does not end to be the product sold, it is likely an essential step to generate a more competitive environment, which leads to lower prices.

The biosimilar competition often influences the originators’ behaviour. For generic small molecules, originators have responded to competition by either maintaining price or reducing it based on mandatory price regulations. In the Biosimilar classes we have seen a multitude of different behaviours including launching innovative long-acting / pegylated products without a price premium, or effectively reducing the price levels or even entering in the manufacture of biosimilar versions.

The price reduction has different impacts on the usage of biosimilars in different Member States contrary to the experience with small molecules where lower price generally increased the volume uptake. In the case of biosimilars, the price reduction has the biggest impact on usage or increased uptake in countries with originally low usage or availability in the therapeutic classes.

The differences in approved indications are relatively small for HGH and G-CSF, somewhat larger for EPO and the largest for Anti-TNF. As a result, different products are used for different indications which impact the patients for which they compete in the class. This is most obvious in Anti-TNF. Frequency of administration and mode of administration also impact the competition within a class. There are relevant product differentiations in all four classes which impact the product mix.

---

4 A part of the explanation for such behaviour can be that the product classes are hospital products. The hospital market is characterised by a rather strong competition between manufacturers, including on price.
Closing the Translational Gap: Sharing experiences at national level with biological medicines, including biosimilars

Across European Union Member States, the translation of biosimilar medicines into healthcare pathways and integration into treatment and procurement marks the progress of biosimilar medicines in Europe. Prof Mondher Toumi from Aix Marseille University, France, who moderated this session, noted that biosimilar policies across Europe remain extremely heterogeneous, suggesting that this would affect prices and, ultimately, market penetration. The session was designed to give an overview of developments regarding biosimilar competition, experiences with the use of biosimilar medicines at national level and initiatives undertaken to build understanding and share best practice. Panellists provided examples of how they have approached questions around training and education, patient consultation, switching, monitoring/registries and procurement, when incorporating biosimilar medicines in their healthcare systems. Four countries were selected to share experiences and real world evidence studies with biologic medicines, including biosimilar medicines.

Dr Vito Annese from Careggi Hospital Florence, Italy, presented the findings of PROSIT-BIO study, to date one of the largest studies on switching to or first time use of biosimilar infliximab in over 500 patients with inflammatory bowel diseases. The preliminary result showed that the safety and efficacy profile of the biosimilar seemed not to be different from the originator. While each of 20 regions in Italy may have different rules for their health service provision, the majority of them promote the use of biosimilars in naïve patients, but not in terms of an automatic substitution. Dr Annese expressed concern that with the increasing availability of several biosimilars of the same originator the future in Italy would become even more confusing for patients and doctors since a uniform regulation on biosimilars use is lacking.

Kevin Klein MSc and Dr Pieter Stolk representing Utrecht University, The Netherlands and Lygature/the Escher Project, presented their 'Analysis of Information-Recording Systems in Clinical Practice and Spontaneous ADR Reports', a study about the traceability of biologics after the implementation of the new pharmacovigilance legislation.

It was concluded that an important factor for the limited traceability of brand names and batch numbers for biologics in ADR reporting are the shortcomings in the recording of this information in clinical practice. The study showed that efforts to strengthen the systems for information recording and sharing in clinical practice are needed. A survey among hospital pharmacists in The Netherlands indicated that brand names are not routinely recorded, whereas batch numbers are poorly recorded. Furthermore, a survey among community pharmacists revealed that while 91% indicated that they had recorded the brand name, only 4% undertake efforts to record the batch number. In addition, awareness can still be increased
as 41% of the respondents of the survey were unaware of the requirement to include the batch number in Adverse Drug Reports (ADR) and 18% of the respondents were unaware of the requirement to include brand names for biologics in ADR reports. Finally, it was proposed to carry out additional case studies in different Member States to help mapping EU differences, commonalities and potential success factors for interventions to improve traceability for biological medicines.

**Dr Fraser Cummings, consultant gastroenterologist at the University Hospital of Southampton NHS Foundation Trust, UK**, showcased switch data with infliximab from a study with patients with inflammatory bowel disease. The study is a valuable example for incentivisation of all involved parties. The switch to the biosimilar product allowed Dr Cummings to treat more patients, expand his team and still manage savings of 60-80,000 GBP per month. A very important element was to actively involve patients and build trust between them and the healthcare providers, including nurses. A patient panel for a detailed information and discussion was set up, patients were given the opportunity to discuss the switch with the medical team "in meaningful conversations" and agree in advance. Dr Cummings recorded some side effects but no critical adverse events during the study.

**Dr Krisztina Gecse, gastroenterologist at the Department of Medicine, Semmelweis University in Budapest, Hungary**, conducted a prospective, nationwide, multicentre, observational study to analyse the efficacy and safety of CT-P13 infliximab in patients with Crohn’s disease and ulcerative colitis. It was concluded that real life experience with biosimilar infliximab CT-P13 suggests high response and remission rates similar to those reported earlier with the originator. The adverse events profile and rates were also comparable with those of the originator. Furthermore, Gecse noted that induction treatment with the CT-P13 biosimilar IFX was less effective in patients previously exposed to the originator compound and adverse events are more common in patients with previous exposure to the original compound. Gecse added that there was an assumed price discount with biosimilars for Crohn’s Disease in Hungary of around 25%.

Dr Gecse also cited an EU-wide survey from 2015\(^5\) which revealed that only 19.5% prescribers in Hungary have little or no confidence in biosimilars, compared with 63% in 2013.

Closing the Information Gap: Information and communication needs of patients and healthcare professionals

This session aimed at highlighting the information and communication needs of patients and healthcare professionals focusing on the individual/clinical practice but also on to the policy level, which includes professionals’ education.

In his introductory note, Prof Arnold Vulto, Erasmus University Medical Center, Rotterdam, The Netherlands, presented on the societal need for biosimilar medicines to tackle high budget pressures. If we want our healthcare systems to remain sustainable, also in the future, biosimilar medicines will play a key role, he said. The lack of a solid knowledge base amongst prescribers and patients alike is the main reason why biosimilars are not being used enough. He called for trust building measures to be introduced, emphasising that the European Medicines Agency’s scientific opinion and regulatory evaluation is based on a thorough assessment of the data package including full comparability assessment.

Salvatore Leone, Vice President of the European Federation of Crohn’s & Ulcerative Colitis Associations and CEO of the Italian Inflammatory Bowel Diseases Association, pointed out the necessity to get patients involved in the decision-making process in order to realise patient centred-care. He added that patient-physician dialogue was crucial to achieving “co-owned results” and improving communication and mutual understanding. While he agreed on several issues relating to budgetary concerns, Salvatore Leone cautioned about switching to a biosimilar product if the patient was comfortable with the current treatment as it often takes several attempts to find the right treatment that will suit an individual patient.

With regard to biosimilars, information and education will not be enough, conveyed Prof Vulto the message sent by René Westhovens President of the Royal Belgian Society of Rheumatology, emphasising that beliefs and perceptions must also be addressed. Biosimilars represent one of the many means of achieving savings – including choosing alternative medicines, introducing and supporting responsible prescribing etc. Moreover, biosimilars must not be considered in isolation, but consideration should also be given to reducing the cost of innovator drugs, among other things. Two of the most important factors physicians need in order to be able to take a responsible decision, are unbiased information and shared decision making with patients. This requires time which is often tight. He added that generally and not only with regard to biosimilar medicines, is trust building always a rather longish process.

Jamie Wilkinson, Director of Professional Affairs at Pharmaceutical Group of the EU, representing community pharmacists, explained how his organisation viewed the role of

---

6 Prof West ovens could not participate personally in the conference, but Prof Vulto presented his slides.
Dieter Wiek, Chairperson of the Standing Committee of PARE, which is a contributing party to the European League Against Rheumatism (EULAR), stressed the importance of patient and physician information on biological medicines, including biosimilar medicines. He acknowledged that biosimilars offer more treatment options to physicians, wider access to patients and increased choice, but patients have to get a better understanding of switching and interchangeability of biological medicines and be informed of all treatment options. Patients need lay summaries of recommendations on biosimilar medicines, relevant studies, trials and reviews. Wiek noted that in some west European countries patients are switched to biosimilars because of cost containment reasons and an appropriate shared-decision process was lacking. He demanded data collection for “at least a couple of years” to see what happens in switches to biosimilars.

Update on the Revised Q&As on Biosimilar Medicinal Products for Patients

In order to provide patients, doctors and payers with adequate information on biosimilar medicinal products, the European Commission established 2010 a project group bringing together different stakeholders (patients, physicians, payers, industry and in close cooperation with the European Medicines Agency) who prepared the consensus information paper on biosimilars "What you need to know about Biosimilar Medicinal Products"s. The document was published in 2013 together with specific Q&A parts for patients, physicians and payers. In 2016 the European Commission decided to launch an update of the Q&A for patients. Emma Woodford, Hibou Consulting, who was commissioned to co-lead on the revision process and draft the updated version gave an overview on the state of play of the revision. The update process was very much focused on consultation with patient representatives in order to address their priorities in a language that is easily understandable.

---

7 Process on Corporate Responsibility / Access to Medicines in Europe including a Working Group on Market Access to and Uptake of Biosimilars

8 http://ec.europa.eu/DocsRoom/documents/8242/attachments/1/translations
despite the fact that it is a highly complex, scientific concept. The leaflet for patients was published together with this report and is available at the European Commission's website.9

**Closing remarks**

In her summarising speech Nicola Bedlington, Secretary General of the European Patients’ Forum urged a continued multi-stakeholder approach on biosimilars at EU level, noting, nevertheless, fundamental differences of opinion on biosimilars switching, labelling, extrapolation, etc. that still exist. She stressed that, from a patient perspective, the availability of biosimilars would be instrumental in expanding access to treatments for many diseases, while easing budgets. Nicola Bedlington also cited studies from Hungary and the UK in which real world evidence on biosimilars – including on switching – is being collected. Building the evidence base helps patients and clinicians to take an informed and shared decision.

The European Commission, Directorate General Internal Market, Industry, Entrepreneurship and SMEs, would like to thank to all stakeholders, speakers and participants for their commitment to contribute to the multi-stakeholder discussions at European and national level. The Commission intends to organise a similar stakeholder event in 2017.