Biosimilars: European Payer Perspectives (2016)
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### The current regulatory environment

**Key insights**

1. Regulatory data requirements mostly satisfy payers, but some would prefer additional clinical comparability data and information on interchangeability.
2. Small, clinically non-significant differences between biosimilars and their reference products are permissible.
3. Real-world, interchangeability data could provide assurance that biosimilars are comparable to reference products.

### Recent policy events shaping the biosimilars market

**Key insights**

1. EMA’s guideline on biosimilars goes into effect, provides guidance on clinical trial comparators.
2. European Biosimilars Group asks EFPIA to clarify its policy on off-patent biological drugs.
3. NHS England position statement seeks to define concept of biosimilar medicine.
4. Ireland’s HPRA published guide on biosimilars, outlining recommendations for indication extrapolation and interchangeability.
5. Finland’s Fimea proposes hospital-level interchangeability, but rules against pharmacy-level substitution.

### Biosimilar naming rules

**Key insights**

1. Payers argue benefits of existing name proposals, suggest alternative traceability strategies.
2. Payers express concern that WHO’s Biological Qualifier proposal could add layer of confusion.
3. Biosimilar naming should promote traceability without drawing attention to differences, payers suggest.
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Research objectives and methodology

Objectives

Following on from our January 2015 Biosimilars: European Payer Perspectives report, this FirstView advisory update provides an overview on how payers' opinions on the core issues facing the European biosimilars market have changed over the past 12 months. While much progress has been made across the past year to improve perceptions of biosimilars among physicians and patients alike, significant challenges remain on key market-shaping issues, including indication extrapolation and switching policies, traceability and naming initiatives, and pricing strategies. While payers concede that the majority of these barriers to adoption are becoming more surmountable, it is imperative that biosimilar developers and originator companies alike understand the current biosimilar landscape, including how new and existing opportunities and uncertainties could shape the future biosimilars market. Key questions that were asked during the course of the research included:

- From the payers’ perspective, how have levels of awareness of, familiarity with and acceptance of biosimilars at the payer, physician and patient level changed across the past 12 months in Europe?
- How have the key drivers and resistors of biosimilar usage in Europe evolved over the past year?
- Do payers agree with the current European regulatory pathway for biosimilars, and how do they perceive it changing in the years ahead?
- How do payers expect pricing dynamics within the European biosimilars market to evolve, and what are their expectations in relation to the pricing of originator biologics in response to biosimilar competition?
- How have payers’ views in relation to the key market shaping issues of switching, automatic substitution, extrapolation of indications and biosimilar naming changed over the past year?
- What are the critical success factors for the European biosimilars market, both from a biosimilar and originator biologic manufacturer perspective?
Methodology

The analysis contained in this report is based primarily on the insights and opinions of 15 expert payers from each of the major European markets (i.e. EU5: France, Germany, Italy, Spain and the UK; three interviews per market). English-speaking payers were recruited from France, Germany and the UK; interviews in Italy and Spain were conducted in the local language. All respondents received a financial incentive to take part in the research. To qualify, respondents had to meet the following screening criteria:

- Between 5-30 years’ experience;
- A pricing and reimbursement (P&R) or health economics expert;
- Responsible for developing, setting or administering medicine reimbursement schemes;
- A primary decision-maker; key influencer or a voting/contributing member on a P&R committee (PRC); or likewise on a drugs and therapeutics committee (DTC);
- Have direct experience of making formulary decisions for biological therapies in at least two of the following areas: oncology, rheumatology, gastroenterology, dermatology, endocrinology, neurology, nephrology or fertility;
- Direct experience of assessing biosimilars for inclusion on formulary, either as part of a committee or as the lead decision-maker.

Details of each payer interviewed can be found in the appendix.

Interview questions were designed to evaluate how the biosimilars market has changed during the past 12 months, as well as the future marketplace for biologics and biosimilars in Europe with regard to pricing, reimbursement and market access. Primary market research was complemented with in-depth secondary research across multiple, publicly available sources of information. Data from other FirstWord reports were also used, including FirstView’s Biosimilar Index (version 22, updated 16 December 2015).

Small, clinically non-significant differences between biosimilars and their reference products are permissible

For some payers, proving that a biosimilar was non-inferior to its reference product was enough to support approval. Others, meanwhile, suggested that small, non-clinical differences were permissible – and even expected – given the nature of the biosimilar manufacturing process and the fact that reference products differ slightly from one batch to another. They noted that despite these differences, however, the biosimilar should still demonstrate the same safety, efficacy and immunogenicity.

“In my eyes, non-inferiority is OK. But of course, it is better to show, in a range, how close are the clinical outcomes to the branded product? But this discussion is sometimes a little bit crazy, because also the branded products change over the years, their production and processes, and the branded product is not the same as the branded product that first got an approval. So I guess the EMA is on a good path, and for me it is working.” GERMAN PAYER

“I think small clinical differences are permissible, because you are always going to get that slight change maybe in the state of configuration, or in the glycosylation process – we accept that. But as long as it doesn’t affect the adverse event profile or the clinical outcomes, non-inferiority is going to have to be fine, because to do superiority studies, you are going to need massive numbers of patients and it is going to be cost-prohibitive to [biosimilar manufacturers] to do that kind of study.” UK PAYER

“It has to be the same. It has to have the same efficacy and safety. But small non-clinical differences are permissible, such as the fact that the molecule is not exactly the same. What is not acceptable are differences in terms of safety, immunogenicity, efficacy, the form of administration, the doses.” SPANISH PAYER

“There are bound to be small differences, but if you look at infliximab, the one thing that everybody said all the time was ‘Well of course, infliximab is actually a biosimilar of itself because it has changed, it is on its 40th reiteration’. So small changes are acceptable in these big molecules. Really, it is about the actual effect and the safety.” UK PAYER

“For me, the level of difference is not that important. What I am interested in is the efficacy. The efficacy must be either similar or the same, not inferior because the manufacturers of the originators have insisted that the production of biotechnological drugs, when you change sites, will generate differences. But then there will be differences between batches too even by the same manufacturer. So I am not that interested in the difference, as long as it is minimal, of course. What I am interested in is that during the registration phase of this drug, the efficacy must be the same or superior.” ITALIAN PAYER
**Biosimilar company experience and location**

One misinformation tactic cited by several payers was for originator companies to cast doubt on the quality of biosimilars based on the clinical experience level or even location of a biosimilar company. Asked whether the actual level of experience a company has in the biopharmaceutical market – or pharmaceutical space in general – had any bearing on a payer’s level of trust in the therapy, the payers wanted to believe that it shouldn’t matter because they must still provide data to prove the safety and efficacy of their biosimilar.

“We are encouraged by what we know about the companies. If we talk about the companies which commercialised the biosimilar, we have such background and such knowledge about these companies, I don’t know how we will consider if tomorrow we have a new company which is only engaged in biosimilar drugs – it will not be the same. Perhaps we will be a little more suspicious.” FRENCH PAYER

“Their reputation is important. Pfizer commercialising a biosimilar is not the same as India’s Aurobindo, for example, doing it. It is not the same. Even if the manufacturer in the end is the same. But for physicians and so on, it inspires a different level of trust.” SPANISH PAYER

“In my eyes [their experience is] not really of concern, because it’s important to make their data transparent, but they don’t need that big clinical experience in my eyes – although we also have the insight, we have the data transparency and we can create our own results.” GERMAN PAYER

“Perhaps [their experience] has a certain value for physicians, perhaps they feel more confident if they know that there is an innovative company behind a biosimilar. It has a weight that is difficult to quantify, but it may have a relative importance for them. For pharmacists, I think it is less important, but for physicians it is.” SPANISH PAYER

“That [lack of experience] is what the originator companies highlight, but I think it’s only of relative importance.” ITALIAN PAYER

“The originator company reputation is not important in Germany. In reality, we would like to see a company who really knows what they are doing – typically they do – but different from generics that may be produced or repacked in a garage. That is not possible in the case of a biosimilar. So I don’t expect there will be a lot of companies; they must have enough money to invest for this production, and so I think it is helpful if it is a company that is experienced in producing drugs like this.” GERMAN PAYER

In the same vein, the payers suggested that the physical location or country of manufacturing of a biosimilar developer should also not hold much bearing, as each company and therapy is subject to the same quality and safety standards, including manufacturing site inspections. A number of payers admitted that there probably were inherent biases, however, either for them, prescribing physicians or even with patients.
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