IMS INSTITUTE FOR HEALTHCARE INFORMATICS

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Delivering on the Potential of Biosimilar Medicines

The Role of Functioning Competitive Markets

Introduction

As biologic medicines play a more significant role in patient care across a growing number of disease areas, the emergence of biosimilar medicines across Europe and in the United States brings the promise of new sources of value. The prospect of more affordable options that are safe and effective opens up opportunities for health systems to expand access to biologics for more patients, free up resources for investment in new areas, and bring relief to pressured healthcare budgets.

Realizing this potential is neither easy nor assured. The lack of uniformity across EU nations that have had access to biosimilar medicines for almost a decade suggests the underlying elements of achieving the full potential from biosimilar medicines are not well understood at a policy level nor implemented effectively at a practical level.

The purpose of this report is to describe the potential role for biosimilars and their contribution to healthcare systems; the risks for stakeholders to realize that full potential value; and the requirements for competitive functioning markets in order to capture the full value. It draws on analysis of trends across EU nations over the past decade and observations of the differing practices undertaken by stakeholder groups.

The study is based on independent research and analysis undertaken by the IMS Consulting Group that was funded by Novartis. The interpretation of the results of the research and analysis and preparation of this report was undertaken independently by the IMS Institute for Healthcare Informatics, also with funding by Novartis. The contributions to this research of Eoin Jennings, Malte Kremer and the IMS Consulting Group are gratefully acknowledged.

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Executive summary

The global biologic medicines market is projected to exceed USD390 billion by 2020, by which time biologics will account for up to 28% by value of the global market for pharmaceuticals. Biosimilar medicines therefore have an increasingly important role to play. By competing with original biologic medicines across a growing range of therapy areas, biosimilars enable stakeholders – including payers, physicians, and patients – to benefit from greater choice when it comes to treatment options.

By 2020, biosimilars have the potential to enter markets for a number of key biologics that have current sales of more than EUR40 billion. The cumulative potential savings to health systems in the five major European Union (EU) markets and the U.S., as a result of the use of biosimilars, could exceed EUR50 billion in aggregate over the next five years and reach as much as EUR100 billion.

Notably, almost 50 distinct biosimilars are currently in development and will likely result in a highly competitive marketplace over the next five years. This represents significant untapped potential – but not all markets are ready to profit from the benefits offered by the forthcoming generation of biosimilar products. In some countries, the actions of payers and policy-makers may be hampering competition in the marketplace. This is because not all stakeholders have understood how to use competition to maximize the benefits offered by biosimilar medicines.

The markets best-placed to capitalize on the benefits of biosimilars are those with a functioning competitive market, where manufacturers are motivated to participate over the longer term, and where physicians are at the heart of the decision-making process. In this respect, education of stakeholders including physicians is critical – but there remains significant variation between countries in terms of how physicians are educated and incentivized, and in terms of how manufacturers are motivated to participate in the marketplace.

Competition lies at the heart of the biosimilar value proposition, driving the virtuous circle of pharmaceutical innovation and healthcare system sustainability. At present, however, the situation across the EU is very heterogeneous, with varying levels of education and incentivization among stakeholders.

A functioning competitive market is therefore needed to deliver sustainability for payers, physicians and manufacturers alike. Germany has been among the most successful in this regard, through the education of physicians and the implementation of measures designed to stimulate biosimilar prescribing. By contrast, Austria's approach – which has seen some biosimilar medicines subject to mandatory price reductions – has had the opposite effect, resulting in some biosimilar products being effectively excluded from the market.

Physicians, patients and payers require balanced and adequate education on the role that biosimilar medicines can play, while payers need to ensure that physicians and manufacturers are properly incentivized to drive uptake of biosimilar products.

Ensuring sustainability for all stakeholders is important. Focusing on price alone risks constraining the longer-term opportunities for savings, by making the market less attractive for manufacturers, reducing incentives to invest in the development and commercialization of subsequent waves of biosimilar products. By driving out competition, payers may lose out on the price-based savings they are seeking. Furthermore, the focus on price and acquisition cost at the expense of volume risks stifling competition in the marketplace, reducing the level of physician choice and potentially limiting patient access to treatment. Above all, payers need to understand that a focus on acquisition cost rather than volume may appear attractive, but in the longer term will prove to be self-limiting - if not self-defeating.

The potential for biosimilar medicines

- Biosimilar medicines have the potential to enter markets by 2020 for a number of key biologics that have current sales of more than EUR40 billion
- Cumulative potential savings to health systems in the European Union (EU) and the U.S., as a result of the use of biosimilars, could exceed EUR50 billion in aggregate over the next five years and reach as much as EUR100 billion
- Stakeholder choices expand with the availability of biosimilars, including increased patient access to the same molecule or other medicines: use of biologic treatments has increased by as much as 100% following the availability of biosimilars in the EU
- Almost 50 distinct biosimilars are currently in development and will likely result in a highly competitive marketplace over the next five years
- Biosimilars can bring improvements to patient outcomes by providing more treatment options to physicians and reducing the need for rationing
- Substantial untapped potential from biosimilars exists across the EU reflecting different policy and implementation approaches

The world of biologic medicines is changing. Over 80 biologic molecules have been launched globally over the past decade, bringing new treatment options to patients across a large number of therapy areas. A global market worth USD46 billion in 2002[1] is projected to grow to USD390 billion by 2020, by which time biologics will account for up to 28% by value of the global market for pharmaceuticals.[2] For payers, however, the growth of the biologics market has presented new challenges, as they seek to preserve access to cutting edge medicines in the face of growing budgetary pressures.

Biosimilar medicines form an increasingly important subset of this global market. By competing with original biologic medicines across a growing range of therapy areas, biosimilars offer stakeholders –including payers, physicians, and patients – greater choice when it comes to treatment options.

2016 marks a full decade since the approval of the first biosimilar medicine in Europe. Sandoz's human growth hormone (HGH) Omnitrope (somatropin) received approval from the European Commission in April 2006, satisfying regulators that this biosimilar medicine offered a safe and efficacious alternative to the original biologic. In so doing, the treatment paved the way for other biosimilar medicines to enter the market across a range of therapy areas.

Ten years on, and it is clear that biosimilar products are set to play a vitally important role in the virtuous circle of pharmaceutical innovation and healthcare system sustainability. The emergence of a greater range of highly competitive biosimilar medicines will generate savings that can be reinvested in healthcare provision, while at the same time driving pharmaceutical innovation that ultimately improves outcomes.

However, while there may be a growing recognition that biosimilars can contribute to solving the problems facing payers and physicians in today's constrained budgetary environment, too few stakeholders – including payers, physicians and manufacturers – have so far taken the necessary steps to create the optimal conditions that would enable them to leverage the potential for greater competition in the marketplace. Without a concerted effort, payers, physician and patients alike risk missing the biosimilars opportunity.

The Near-Term Opportunity for Biosimilars

The current size of the biologics market for those products losing patent exclusivity between 2015 and 2020 is significant. The combined value in the year to September 2015 of the eight top-selling biologic medicines losing exclusivity protection from patents or other measures between 2015 and 2020 cross the EU5 (France, Germany, Italy, Spain and the UK) and the U.S. was EUR42.3 billion (see Exhibit 1). These include products in two major therapy areas:

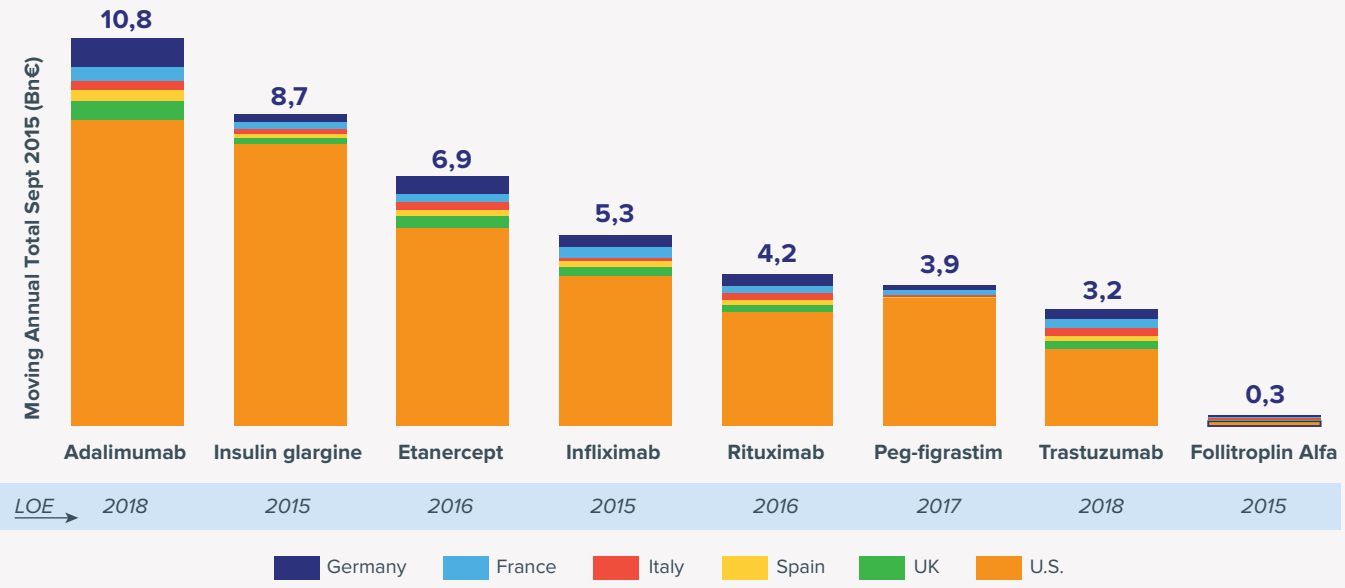
Inflammation

- Humira (adalimumab), for multiple inflammation indications, including rheumatoid arthritis (RA), Crohns' disease and psoriasis among others, with sales of EUR10.8 billion in the EU5 and the U.S. Loss of exclusivity (LOE) in the U.S. as well as the EU is currently expected in 2018.[3]
- Enbrel (etanercept), which is used in the treatment of a number of chronic inflammation conditions, including RA, plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, and juvenile idiopathic arthritis (JIA). Sales of EUR6.9 billion across the EU5 and the U.S. in the year to September 2015. LOE in the EU is expected in 2016 and in 2028 in the U.S.

Diabetes:

- Lantus (insulin glargine) for type I and type II diabetes, with sales of EUR8.7 billion in the EU5 and the U.S. in the year to September 2015. Lantus lost exclusivity in the EU in 2015.

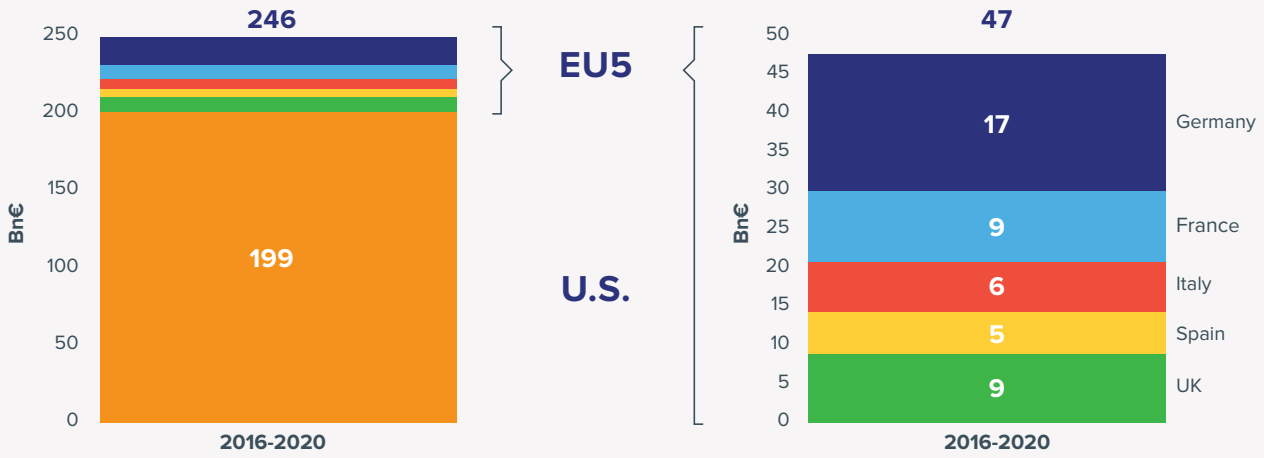
Exhibit 1: EU5+U.S. Sales of Key Biologics Scheduled to Lose Patent Protection in 2015–2020



Source: IMS Health, MIDAS, Dec 2015

For payers, this is a significant target to aim at. As can be seen in Exhibit 2 below, cumulative spending in the EU5 on the eight originator biologic medicines identified above is expected to reach EUR47 billion over the period 2016–2020, in the absence of any biosimilar competition.

Exhibit 2: The Addressable Biosimilar Medicines Market in the EU5 and the U.S., 2016–2020



Conversion rate: 1 USD = 0.916562 EUR (01/20/2016)

Source: IMS Health, MIDAS; IMS Health Market Prognosis; IMS Institute for Healthcare Informatics, Dec 2015

Notes:
Addressable market is calculated based on projected growth of originator market without biosimiliar entry.
Growth rate is based on historical growth and analogue analysis.

The potential savings opportunity provided by biosimilars comes to European payers in particular at a time of ongoing budgetary pressures. The constrained payer environment is triggering a range of initiatives designed to limit growth in healthcare budgets and in many cases target pharmaceutical budgets specifically (see Box 1).

Box 1: The Constrained Payer Environment

France

The 2016 draft social security finance law (projet de loi de financement de la sécurité sociale, PLFSS) includes a range of initiatives designed to reduce the overall deficit of the social security system (excluding pensions) from EUR9.0 billion in 2015 to EUR6.0 billion in 2016.

The annual target growth rate for healthcare spending (Objectif National de Dépenses d'Assurance Maladie, ONDAM) is to be set at 1.75% in 2016. To achieve this target, the legislation outlines healthcare sector savings of EUR3,410 million, including of EUR1,580 million in relation to pharmaceuticals.

Italy

As provided for by the 2015 Stability law, healthcare savings of EUR2.352 billion are to be made in 2015, based on the measures included in this and any others implemented at the regional level.

Spain

In October 2014, six autonomous communities (CAs) – Baleares, Canarias, Cataluña, Extremadura, Murcia and Valencia – had already exhausted their pharmaceutical budgets for 2014, and had to rely on credit line funding from central government in order to pay pharmacy invoices.

Subsequently, in January 2015, the Treasury expressed concern that seven CAs – Castilla-La Mancha, Castilla y León, Cataluña, Extremadura, La Rioja, Murcia and Valencia – were at risk of being unable to pay their pharmaceutical invoices in 2015. According to the reports, the Treasury's concerns are based on the fact that for each of these CAs, pharmaceutical budgets for 2015 are lower than official estimates on total spending on pharmaceuticals in 2014.

UK

The National Health Service (NHS) in the UK faces significant funding challenges over the coming years. Notably, an October 2014 report by NHS England and Monitor (the health services regulator for England), warned that the NHS faces an annual funding shortfall of GBP30 billion by 2020/2021.

While payers cannot expect to realize all of the net savings resulting from the availability of lower cost biosimilars, the extent to which they are able to redirect spending toward greater patient access, new generations of innovative treatment, and budgetary relief, depends on their policy approaches to the biosimilar marketplace.

Potential Savings from the Use of Biosimilars

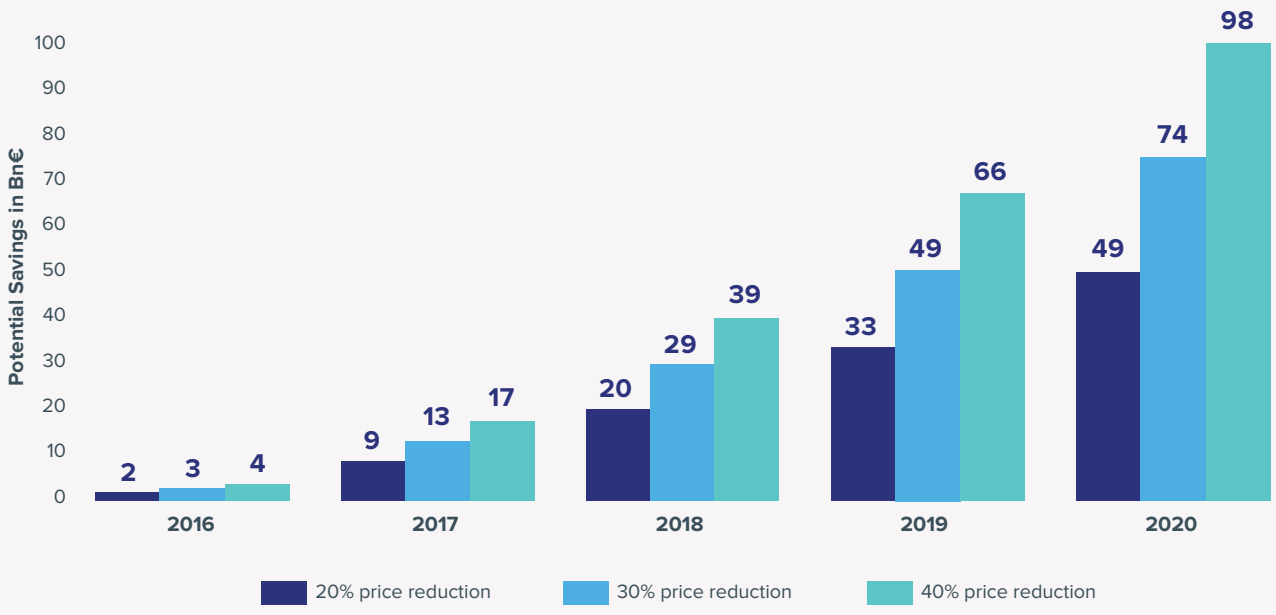
By opening markets to biosimilar competition, healthcare systems could realize savings of more than EUR10 billion in the EU5 alone between 2016 and 2020, simply based on direct competition for the originator molecule and excluding any indirect competition for other in-class or therapy-area specific product sales.

The potential is clear. A 30% reduction in price per treatment day across eight key originator biologics scheduled to lose exclusivity in 2016-2020, driven by biosimilar competition in the marketplace, could yield cumulative savings for European healthcare systems of about EUR15 billion over the next five years.

The cumulative savings over the next five years in the EU5 and the U.S. combined could range from EUR49 billion to as much as EUR98 billion (see Exhibit 3).

The extent of the actual savings realized – where payers end up on this spectrum – is dependent on policy development and implementation across all stakeholders in the healthcare system.

Exhibit 3: Biosimilar Savings Potential in the EU5 and U.S., for 8 Key Products in 2015-2020



Source: IMS Health, MIDAS, IMS Health Market Prognosis; IMS Institute for Healthcare Informatics, Dec 2015

The Expansion of Stakeholder Choice

Encouraging the use of biosimilar medicines enables stakeholders, including payers, physicians, and patients, to benefit from the greater choice on offer. By encouraging the use of biosimilar medicines as alternatives to originator biologics, payers benefit by saving and can reinvest these savings to:

- Expand access to the same molecule
- Expand access to other medicines

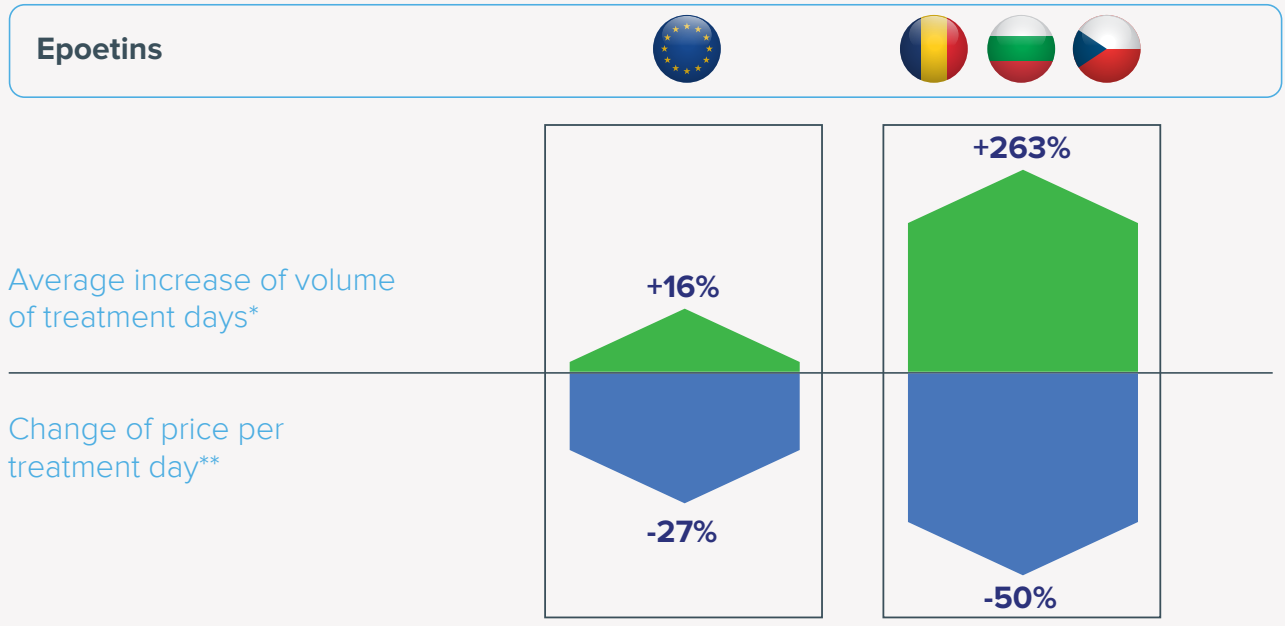
Physicians also benefit from this choice by being able to choose the treatment that best suits a patient's needs.

Expanding Access to the Molecule

Across the EU, the use of erythropoietins (EPOs), granulocyte-colony stimulating factors (G-CSFs) and human growth hormone (HGH) have all increased following the launch of biosimilar versions (see Exhibit 4).

This increase in usage was heavily driven by the availability of biosimilars as well as other factors, such as expanded indications. Notably, in markets where access to these molecules was previously restricted, for example Romania, Bulgaria, and the Czech Republic, average uptake of EPOs increased by over 250% following the introduction of biosimilars – primarily driven by the presence of treatment options not previously available.

Exhibit 4: Increase in Biologics Market across EU following Launch of Biosimilar



Source: IMS Health, MIDAS, The Impact of Biosimilar Competition, Nov 2015

Notes: Pricing and discounts: the report is based on publically available prices. Discounting occurs, especially in contracting with hospitals and in countries using tenders for biological drug procurement, which can lead to larger price fluctuations than is visible through the reported IMS Health data.
* Change of volume of treatment days in total market between launch and 2014.
**Change of price per treatment day in total market between launch and 2014.

The experience of Neupogen (filgrastim) in the UK is instructive. Filgrastim is G-CSF used in the treatment of infection and neutropenic fevers in patients undergoing chemotherapy. Following the launch of the first biosimilar version of the medicine in November 2008, a number of Strategic Health Authorities (SHAs) in England opted to reassess their existing guidance relating to the use of G-CSF medicines.

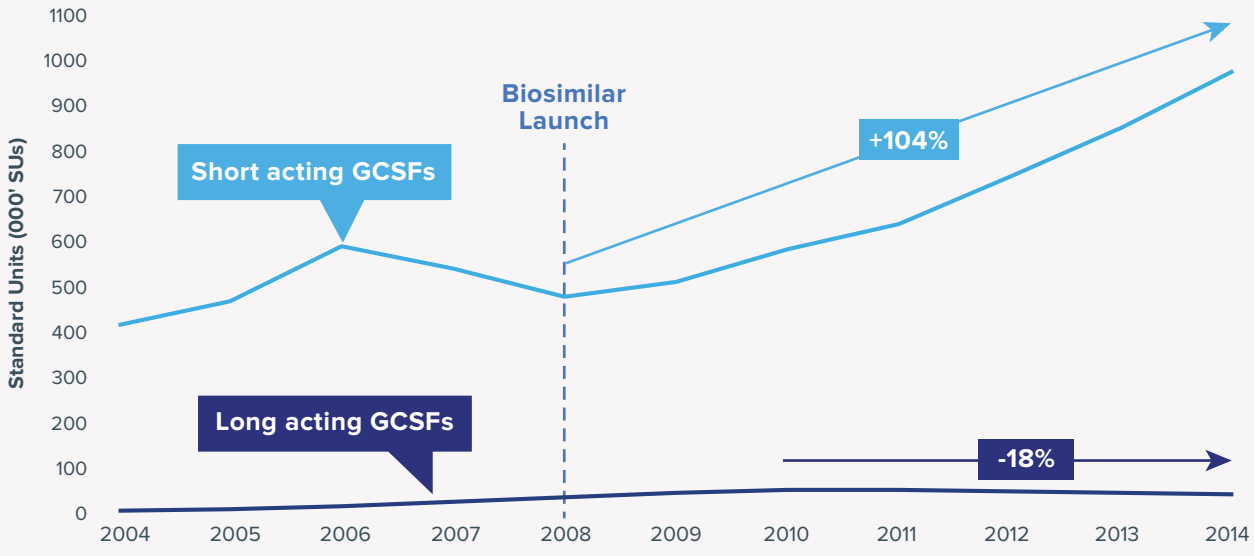
The guidelines were updated to reflect the improved cost-effectiveness of biosimilar filgrastim versus alternative treatments; as a result, G-CSF was moved to first-line cancer treatment.

The impact of this change was pronounced in that overall uptake of filgrastim (both original and biosimilar) increased markedly. Indeed, in the period between January 2009 (shortly after the launch of the biosimilar) and January 2014, overall consumption of filgrastim short-acting (SA) increased by 104% (see Exhibit 5).

This increase represents a significant cohort of patients who otherwise may not have been able to access treatment with the molecule. By giving physicians, payers, and patients greater choice in the range of treatment options available, the launch of biosimilar filgrastim ultimately enabled a greater number of patients to be treated with this important therapy in a more cost effective manner than before.

It can be inferred from this that the launch of biosimilar G-CSF also led to improved patient outcomes, by enabling greater numbers of patients to access these treatments at an earlier stage of the therapy cycle.

Exhibit 5: Filgrastim Uptake in the UK



Source: IMS Health, MIDAS; IMS Consulting Group, Nov 2015

Notes:
Changes in development are depicted as overall changes in % between 2008 – 2014 (short acting) and 2010-2014 (long acting). UK market only.

Expanding Access to Other Medicines

Biosimilar medicines also give stakeholders choice in other ways, ultimately improving the options available to both physicians and patients.

It has been clear for some time in the small-molecule market that the launch of generic medicines has forced manufacturers to be more innovative, driving research on product development in specialty care, and rare and terminal diseases. Today, society has a broader choice of therapies across a broader range of diseases, and patients benefit from improved outcomes.

The rise of biosimilar medicines offers the opportunity to drive the same level of innovation in the biologics market. By encouraging manufacturers to innovate, the presence of biosimilar medicines in the market increases choice for patients and physicians. Furthermore, the presence of biosimilar medicines actually enables patients to access these innovative treatments – because the use of more cost-effective biosimilar products frees up funds that can be spent on securing patient access to the latest treatments.

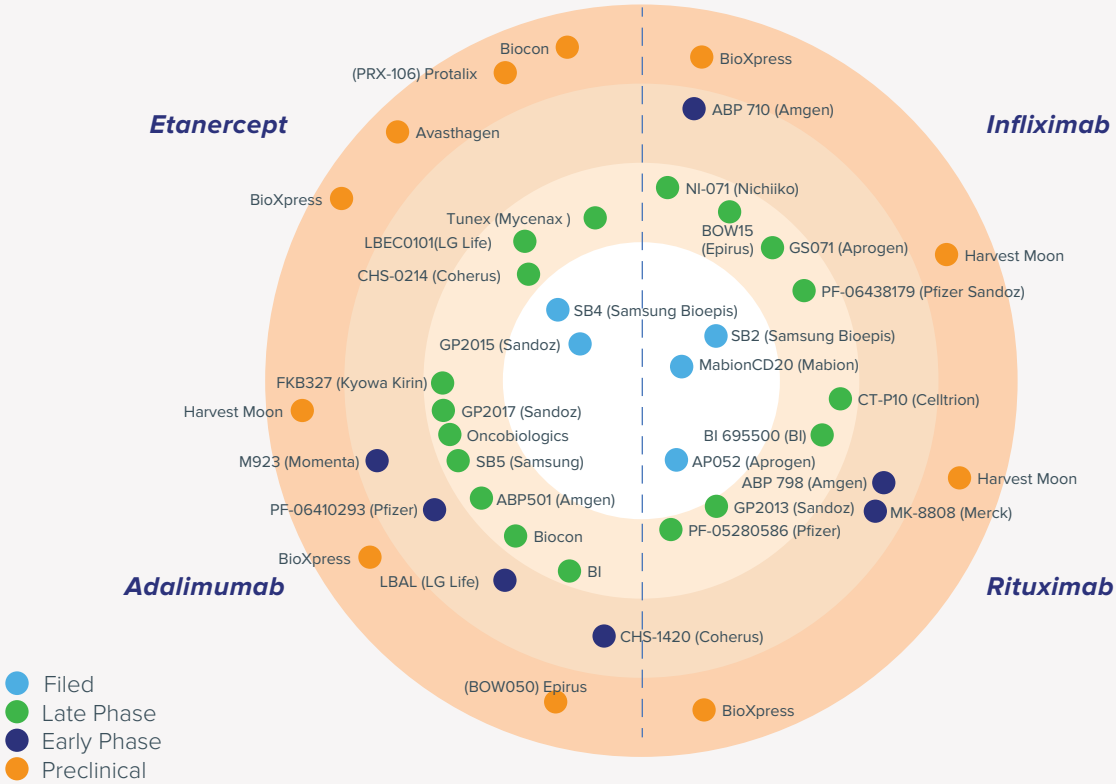
Greater Choice Offered by Biosimilars

At the end of 2015, there were some 41 biosimilar medicines in the pipeline for four key original biologics (see Exhibit 6). Manufacturers have filed marketing authorizations globally for biosimilar versions of three top-selling biologics (while biosimilar infliximab is already on the market in the EU, following the launch of Celltrion's Remsima/Inflectra in late 2013):

- Remicade (infliximab): Samsung Bioepis has filed with the European Medicines Agency (EMA) for its biosimilar infliximab. This will be the second biosimilar infliximab to be approved in the EU, following the launch of Celltrion's biosimilar infliximab.[4]
- Enbrel (etanercept): Samsung Bioepis filed with the EMA in January 2015 for its biosimilar etanercept, the first biosimilar version of Enbrel to seek regulatory approval in Europe. The EMA delivered a positive appraisal in November 2015 under the Benepali brand name, with approval by the European Commission (EC) following in January 2016, paving the way for the launch of the product across the EU. Furthermore, in December 2015, the EMA accepted Sandoz's submission for its biosimilar etanercept; in the U.S., the FDA accepted Sandoz's submission for biosimilar etanercept in October 2015.
- Mabthera (rituximab): Applications have been filed in South Korea and Argentina for marketing authorization for two different biosimilar versions of Mabthera, by Apogen and Mabion respectively.
- Humira (adalimumab): In November 2015, Amgen became the first manufacturer to file an application with the U.S. Food and Drug Administration (FDA) for biosimilar adalimumab (with an application also lodged in the EU in late 2015)– and there are at least half a dozen other biosimilars versions of this molecule in late stage development.

Further biosimilar versions of RoActemra (tocilizumab), Simponi (golimumab), and Orencia (abatacept) are also in development. This pipeline represents an opportunity for payers to realize savings, and for physicians and patients to ensure greater access to these important treatments.

Exhibit 6: Biosimilars in the Pipeline



Source: IMS Health, IMS Institute for Healthcare Informatics, Jan 2016

The Need for Choice

For both payers and physicians, a lack of choice has a detrimental impact on their ability to ensure that patients get the care they need. Where the choice is restricted or constrained, payers may be faced with difficult decisions: between allocating scarce funds for expensive therapies, and denying/delaying certain patients access to treatment if they judge that the costs of the treatment outweigh the likely benefits.

Health systems have struggled with this, creating various additional funding channels and top-up mechanisms. For example:

- In the UK, the Cancer Drugs Fund (CDF) was established in 2010 as a political response to these growing pressures (see Box 2).
- Also in the UK, the National Institute for Health and Care Excellence (NICE) restricts access to many biologic treatments. For example, of 22 selected biologics studied in September 2015 (covering 106 licensed indications), NICE restricted or did not recommend at least one indication for 21 of the 22 assessed biologics.[5] These restrictions may be reversed when lower cost options become available (see Box 3).
- In the Netherlands, expensive medicines have been reimbursed since 2012 via a new "add-on" medicines list for high-cost medicines and orphan drugs, whereby such treatments are reimbursed at a maximum of 100% of the list price (subject to negotiations between insurers and manufacturers). There were 156 medicines on the list as at September 2015.
- Similarly, in France the list of high-cost medicines excluded (liste en sus) from the DRG-based hospital reimbursement system covers some 342 presentations as of October 2015.

Box 2: The Cancer Drugs Fund in the UK[6]

The Cancer Drugs Fund (CDF) was established in October 2010, initially on a trial basis, then on a permanent basis from March 2011. The Fund was conceived as a response to growing public pressure to address the rejection by the National Institute for Health and Care Excellence (NICE) of significant numbers of new cancer medicines; pressure that was exacerbated by a July 2010 report which found that the UK was falling behind other countries in terms of access to oncology medicines.[7] The CDF enables patients in England (but not, notably, in Scotland, Wales or Northern Ireland) to access cancer medicines that have either been rejected by NICE for NHS funding, or which have not yet been assessed by the Institute.

In its first full year, the fund's budget of GBP200 million was underspent, but since then, costs have been rising as more and more patients seek treatment via the Fund. By 2015, annual funding had risen to GBP340 million, but even this has been deemed insufficient to enable the scheme to stay within budget.

The pressures – and need for choice - are only going to become more acute over time. The launch of new active substances provides significant additional benefit to patients, as new treatments are made available that improve patient outcomes. The flip side for payers, however, is that the pressure to provide access to the latest treatments also inevitably puts significant pressure on budgets.

Over the period 2016-2020, some 225 new active substances (NAS) are expected to come to market globally (see Exhibit 7). Many of these products will be launched in the specialty space, and are likely to present payers with significant budgetary challenges. Moreover, it is expected that of these 225 new substances, around 30% will be biologic (both specialty and non-specialty), in line with the general trends observed since 1996 (27% of all new active substances since 1996 have been biologic).

Box 3: The Case of Infliximab for Ankylosing Spondylitis

In 2008, NICE rejected Remicade (infliximab) for the treatment of ankylosing spondylitis (AS), on the grounds that the product was not cost-effective at its list price.

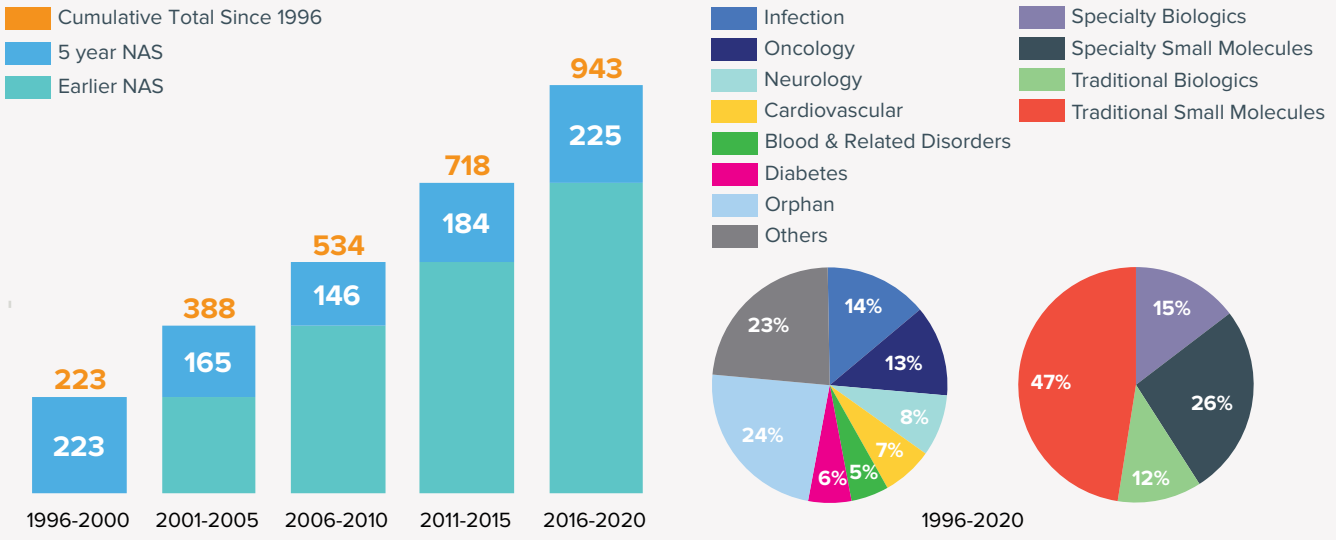
However, in September 2015, NICE issued guidance stating that Remicade, (along with its biosimilars Remsima and Inflectra) were approved as treatment options for adults with AS whose disease has responded inadequately to, or who cannot tolerate, non-steroidal anti-inflammatory drugs (NSAIDs). It is understood that, in coming to this recommendation, NICE considered the acquisition cost of biosimilar infliximab, rather than its list price. The availability of biosimilar infliximab at significant discounts offered through the regional tendering processes has therefore seen this use of acquisition price reverse NICE's previous guidance on infliximab for AS.

Notably, however, treatment with infliximab is recommended only if the patient is started on the least expensive product.

Global spending on medicines is expected to grow at a compound annual growth rate of 4-7% over the same period, to reach up to USD1,430 billion (see Exhibit 8).

Accordingly, with the latest wave of biosimilar therapies expected to come to market by 2020 there is a clear need to grasp the biosimilars opportunity. In this respect, encouraging the establishment of viable competitive markets for biologics and biosimilar medicines is the key to unlocking savings and improving access.

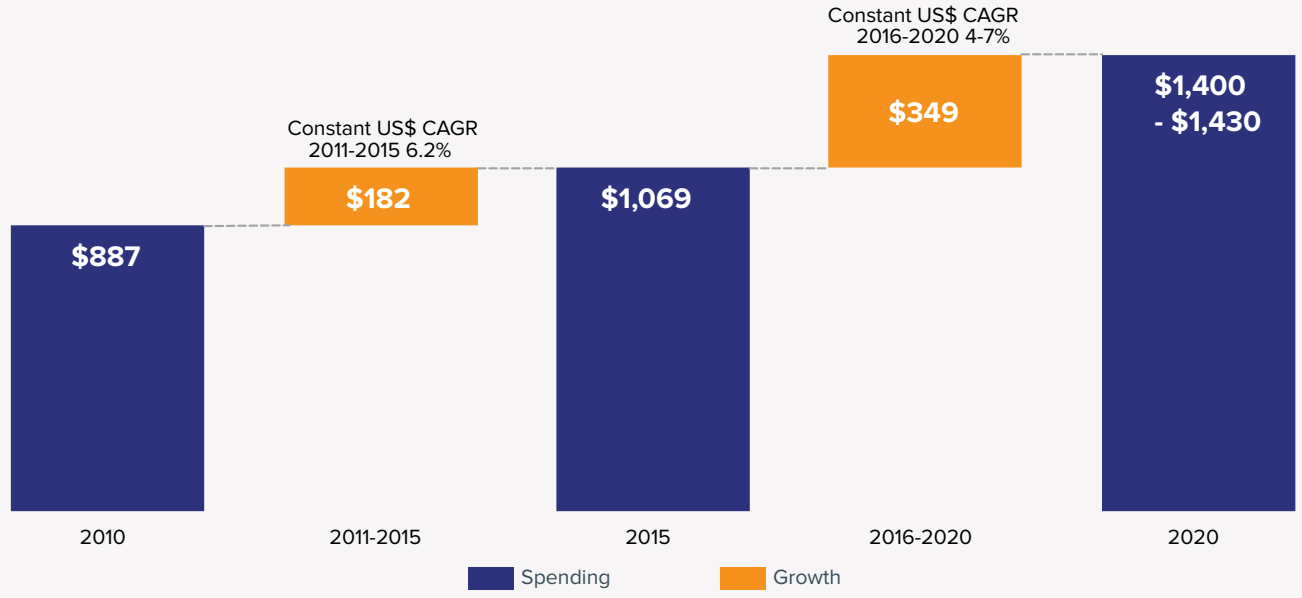
Exhibit 7 : Global New Active Substances (NAS) Available Since 1996



Source: Global Medicines Use in 2020. Report by IMS Institute for Healthcare Informatics, Nov 2015

Notes:
Disease categories based on therapy areas and expected launches 2016-20. Orphan drugs are those to treat small populations with rare diseases, and are defined separately by U.S. FDA and the European Medicines Agency (EMA). Any medicine with an orphan designation for an approved use within the first year after global launch are categorized as Orphan. Half of designated orphan indications are granted more than a year after original approval.

Exhibit 8: Global Spending and Growth, 2010-2020



Source: Global Medicines Use in 2020. Report by IMS Institute for Healthcare Informatics, Nov 2015

Note: Growth in 2011-2015 was reduced by $100Bn and in 2016-2020 increased by $26Bn due to exchange rate effects.

Improvement in Patient Outcomes

While helping ensure health system sustainability – by reducing costs for payers and by facilitating physician and patient choice –the impact of biosimilar medicines on patient outcomes must also be taken into account. Biosimilar medicines help ensure a greater level of competition in the marketplace. Moreover, their presence provides more cost-effective options for patient treatment. As a result, payers can give greater autonomy to physicians, giving doctors greater freedom to prescribe the most appropriate treatments for patients.

For example, in Sweden's Southern Healthcare Region, the launch of biosimilar filgrastim, and the associated reduction in treatment costs for patients receiving G-CSF therapy for febrile neutropenia, prompted the regional authorities to relax restrictions on prescribing. This meant that, while the agreement of three physicians had previously been required in order to commence treatment with the originator product, following the launch of biosimilar filgrastim individual physicians were permitted to prescribe the biosimilar version without the assent of other medical professionals.[8]

As a consequence of this decision, uptake of G-CSF increased five-fold in the Southern Healthcare Region, driven by usage of biosimilar filgrastim. With physicians given the autonomy to prescribe, it can be inferred that this increase was driven by clinical need and that, as a consequence, outcomes improved for patients in the region.

The presence of biosimilar medicines ultimately benefits patients, as they are able to receive the most suitable medicine at each decision point along the diagnosis/treatment pathway. Ultimately, this has the potential to improve overall outcomes for patients.

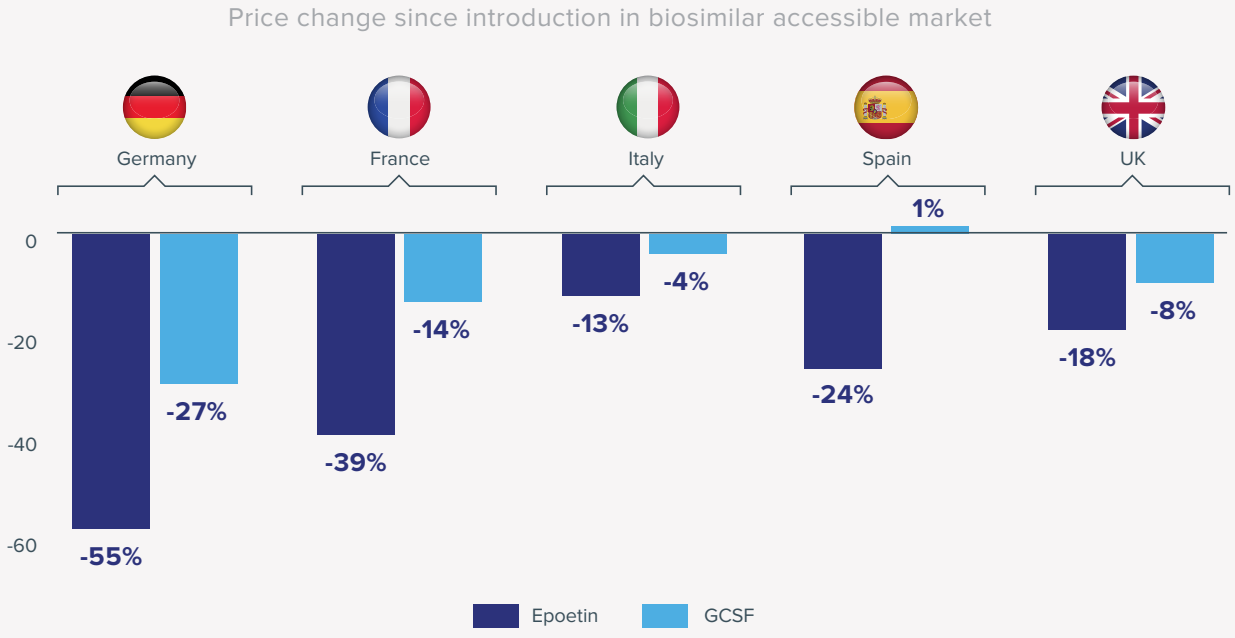
Substantial Untapped Potential from Biosimilars

With new waves of biosimilar medicines ready to come to market in the EU in the next few years, payers and policy-makers need to ensure that they are best positioned to benefit from the untapped potential offered by these treatments.

There is already considerable variation in the approaches adopted by different countries – suggesting that not all markets are ready to benefit from the potential offered by the forthcoming generation of biosimilar products. This existing variation can be seen with reference to the price changes observed in a range of markets following the advent of biosimilar competition. In the EU5 markets, price reductions (across the drug class – i.e. for originators as well as biosimilars) have varied considerably (see Exhibit 9). For example:[9]

- EPOs: In France and Germany, the observed price reduction in the biosimilars accessible market (in 2015) following the introduction of biosimilar competition varied from 39% in France, to 55% in Germany. In Finland, Norway and Sweden, observed price reductions ranged from 25% to 29%.
- Filgrastim: The observed price change (in 2015) for biologic and biosimilar filgrastim, following the launch of the biosimilar version, varied from 14% in France to 27% in Germany. It should be noted that the price level used is gross ex-manufacturer price, which values the product at the level that the manufacturer sells at, without taking into account rebates or discounts.

Exhibit 9: Price and Changes Following Biosimilar Introduction



Source: IMS Health, The Impact of Biosimilar Competition, Nov 2015

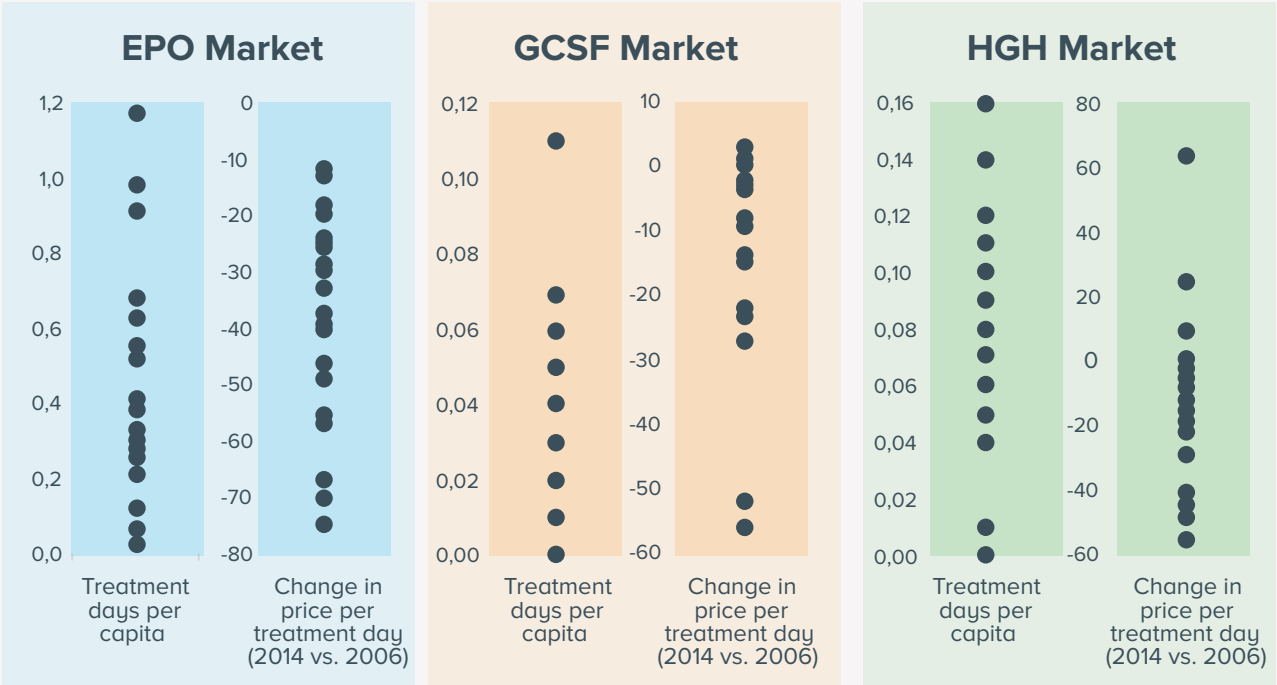
Note: Pricing and discounts: the report is based on publically available prices. Discounting occurs, especially in contracting with hospitals and in countries using tenders for biological drug procurement, which can lead to larger price fluctuations than is visible through the reported IMS Health data.

Similar variation across the EU can be observed when looking at a range of metrics in the EPO, C-CSF and HGH markets (see Exhibit 10):

- Market share versus the reference (originator) product
- Treatment days per capita
- The changes in price per treatment day (2014 vs. 2006) following the launch of biosimilar versions

This variation suggests that the utilization of biosimilar medicines may not be optimized for all products in all markets. Therefore, there is a risk that payers may not be in a position to capitalize on the biosimilars potential as more of these products become available for a wider range of biologics.

Exhibit 10: Variation Across the EU in Market Share, Number of Treatment Days, Price per Treatment Day



Source: IMS Health, The Impact of Biosimilar Competition, Nov 2015

Note: Pricing and discounts: the report is based on publically available prices. Discounting occurs, especially in contracting with hospitals and in countries using tenders for biological drug procurement, which can lead to larger price fluctuations than is visible through the reported IMS Health data.

By opening markets to biosimilar competition, healthcare systems across Europe can make significant savings in this space. This space represents the total potential savings achievable as a result of the onset of biosimilar competition for a range of original biologics. Payers need, therefore to adopt policies that will ensure that they can realize as much of these potential savings as possible.

The key to achieving potential savings lies in ensuring that payers adopt policies that enable optimization of the biologics market by encouraging sustainable competition.

Risks to realizing the benefit of biosimilar medicines

- The actions of payers and policy-makers may be hampering competition in the marketplace
- Not all stakeholders have understood how to use competition to maximize in a sustainable way the benefits offered by biosimilar medicines
- The markets best-placed to benefit from the biosimilars opportunity are those with a functioning competitive market, where manufacturers are motivated to participate, and where physicians are at the heart of the decision-making process
- Inappropriate use of incentives can prevent payers from realizing the potential of biosimilar medicines
- Physicians should not be expected to shoulder the entire burden of education on the clinical, cost and health system benefits of biosimilar medicines
- Manufacturers have been inconsistent in their messaging on biosimilar medicines

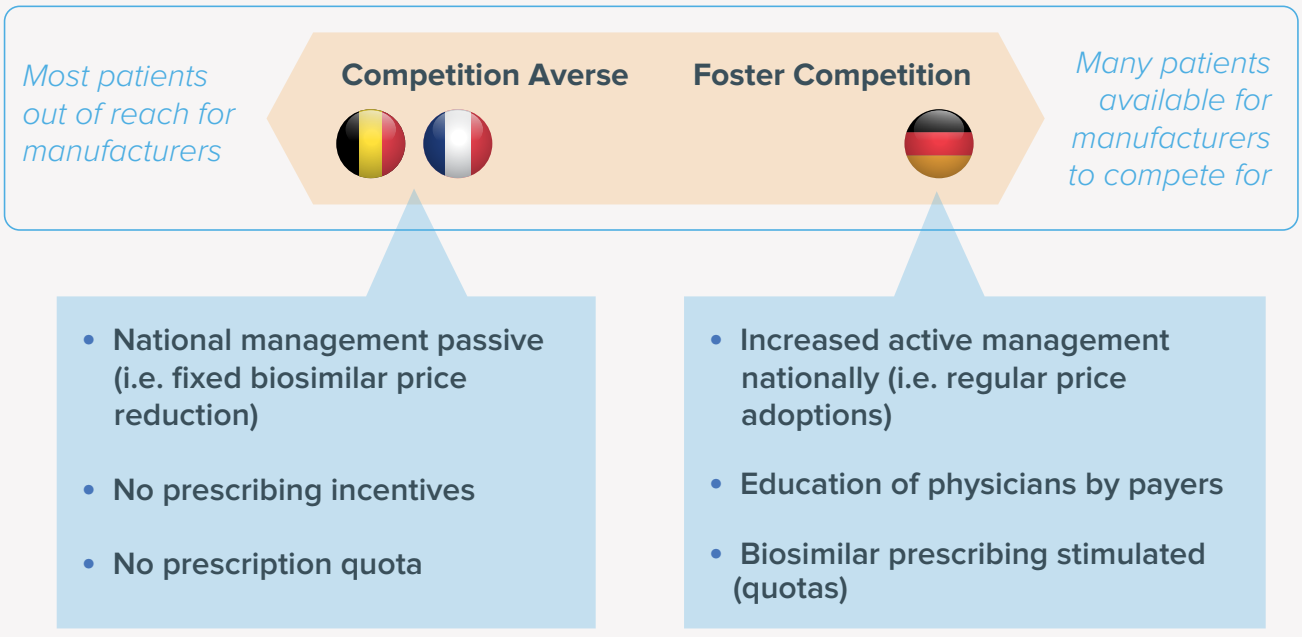
Biosimilar medicines can play a central role in enabling payers to make significant savings over the period 2016–2020 and beyond. However, this potential is at risk.

The importance of adopting a strategy that optimizes the benefits offered by biosimilar medicines cannot be overstated. The story of biosimilar medicines over the past 10 years has been one of slow acceptance, with payers, physicians and patients exhibiting a significant degree of wariness about these new treatments. But this very caution is contributing to the risk that stakeholders will miss the biosimilar opportunity over the coming years. Payers simply cannot afford to further bide their time.

Hampering Competition

There is considerable variation across the EU in terms of payer policy approaches to biosimilars (see Exhibit 11). It can be argued that in terms of supporting competition some markets have made significant strides, but others are being left behind. Sustainable competition is achieved where conditions are optimized to ensure strong biosimilar uptake in the long term, as has been the case in Germany.

Exhibit 11: Payer Biosimilar Policies in Selected European Markets



Source: IMS Health, IMS Consulting Group, Jan 2016

This variation in policy is broadly reflective of the variation in biosimilar use seen across the EU. Taking just one drug class, EPOs, it is clear that there are wide variances in the changes in price per treatment day achieved following the launch of biosimilar versions (refer to Exhibit 6).

The impact of different policies can also be clearly observed in relation to the rate of uptake of biosimilars across the continent. For infliximab, for example, it is clear that some markets have seen more immediate uptake than others.

It is noteworthy that in Norway and Denmark, where physicians have been at the heart of the decision-making process in relation to biosimilar medicines, uptake of biosimilar infliximab was rapid and sustained. These markets demonstrate that trusting and empowering physicians to make the right decisions is a key component of ensuring the longer-term sustainability of the market.

Across Europe, payers have adopted a variety of approaches when it comes to giving physicians and manufacturers a stake in the market:

- Some have sought to encourage physicians to take the initiative on prescribing biosimilar medicines, but others have not.
- A number of countries have recognized the need to motivate manufacturers to fully participate in the market by not restricting the number of patients for which manufacturers can compete. But others have not used this approach – for example setting definitions of what constitutes good biosimilar uptake through the use of targets or ceilings.

Some countries have recently taken initiatives to create a more positive environment towards biosimilar medicines. For example, in Belgium, as part of a new "Future Pact" (Pacte d'Avenir), the government, the pharmaceutical industry and the scientific associations of physicians and hospital pharmacists have signed a convention aimed at encouraging the use of biosimilar medicines in at least 20% of treatment-naive patients. A first evaluation is planned mid-2016 and a final conclusion is expected by the end of 2016. If uptake of biosimilars has not significantly improved by this point, the government has pledged to implement legislation that will make the 20% target mandatory from 2017.

Encouraging Physicians to Lead Decision-Making

There are numerous examples of markets that have sought to encourage physicians to take the initiative in relation to biosimilar medicines (see Box 4).

Motivating Manufacturers

To encourage manufacturers to participate fully in the market, some payers have recognized that they have a role to play in ensuring that:

- A large number of patients are made available,[10] so that biosimilar manufacturers can compete for a significant volume of medicines.
- Manufacturers have predictability/stability in the market.

For example, in Norway and Denmark, all patients (both existing and treatment-naive) have been made eligible for biosimilar use. Physician participation is key to the success of this model. In both Norway and Denmark, the physician is at the center of the decision-making process, and it is physicians – rather than payers or other stakeholders – who have helped to drive uptake of biosimilar medicines in these countries. Importantly, in each of these markets, choice remains in the hands of the physician, who is best positioned to assess the needs of his or her patient.

Inappropriate Incentivization

Where some healthcare systems have chosen to encourage physicians, and/or to motivate manufacturers to participate, others have chosen less effective methods of incentivization. These processes may ultimately become counterproductive, and prevent payers from realizing the potential of biosimilar medicines.

Payers should be aware of the danger of adopting approaches that force manufacturers to compete on price alone i.e. a "one winner takes all" approach. Manufacturers must, of course live with the risks entailed by entering a particular market, but they also endeavor to plan as best they can for such risks. But when forced to compete on price alone, such planning becomes more difficult for manufacturers. A focus on price favors short-term market players seeking a quick return, to the detriment of those seeking to make a longer-term strategic investment.

Box 4: Physicians at the Heart of Decision-Making

Norway

In Norway, the procurement process for biosimilar medicines has thus far largely been perceived as payer-driven – but in reality physicians are afforded a central role in the decision-making process.

The role of the Norwegian Drug Procurement Co-operation (*Legemiddelinnkjøpssamarbeidet*, LIS), which is responsible for organising tenders for the procurement of medicines for state hospitals, is critical. LIS' evaluation panels are comprised of physician experts and representatives from all four of the country's healthcare regions.

In the LIS model, physicians take into account a range of factors, both clinical- and cost-related, when deciding to award a tender to a particular product. As a result, it is physicians who have driven the uptake of biosimilar medicines in the market.

In addition, as state hospitals are funded via a DRG-system, which includes the cost of the medicines, hospital physicians are clearly able to observe the benefits of the reduced costs associated with biosimilar medicines. This incentive, combined with the trust that hospital physicians have in the LIS evaluation system, helps further drive biosimilar uptake.

Denmark

In the Danish model, the Council for the Use of High-Cost Hospital Medicines (RADS) has a role similar to that of LIS in Norway.

Spain

In Spain, prescribing indicators have been introduced in some regions. These form part of the targets for physicians to prescribe biosimilars. Where the indicated target is reached, physicians get financial incentives and benefits that can range from more training to benefits within the internal organization.

Italy

In Italy, a number of regions have introduced a system whereby 50% of the savings generated from biosimilar uptake are reallocated to augment by 20% the budget dedicated for coverage of innovative medicines.

Germany

In Germany, the statutory health insurers and physician associations have been proactive in reaching out to physicians in order to encourage them to prescribe biosimilars.

Physicians were approached by their Kassenärztliche Vereinigung (KV, regional physicians' association) early on, using open communication channels and discussion forums to build trust in the biosimilar concept. In addition, prescribing quotas were put in place immediately which were explained to doctors using doctors letters (Ärztebriefe). KVs combined these quota-enforcing "dear doctor" letters with separate letters explaining the potential impact of biosimilar medicines (i.e. in terms of supporting a sustainable healthcare system and ensuring savings for payers).

Consequently, KV enforcement and education campaigns highlighting the savings potential of biosimilar medicines proved to be valid tools to foster competition and increase uptake, especially at times when trust in biosimilar medicines is still being built.

Eastern Europe

In many Eastern European markets, biologics uptake has historically been low, partly due to reasons of cost. However, these markets have seen significant uptake of biologic molecules once biosimilar versions have become available. The inference in this case is clear: physicians will, given the opportunity, prescribe biosimilar medicines if it enables them to reduce costs and thus improve treatment options for their patients.

Box 5: Disincentives for Biosimilar Medicines

Biosimilars Reimbursement in Medicare in the U.S.: The J-Code Problem

In the U.S., the Centers for Medicare and Medicaid Services (CMS) reimburse physician-administered medicines on a "buy and bill" model. Products are reimbursed at Average Sales Price (ASP) - the average ex-factory price, net of any rebates and discounts, to all purchasers in the United States, including wholesalers, retailers, health maintenance organizations (HMO)s, hospitals, government entities, and Medicare Part D providers - plus a specified margin (4.3%).

However, for the first six months following launch, products are not assigned an ASP. Rather, a different benchmark – Wholesale Acquisition Cost (WAC) – is used, which does not take into account the impact of discounts and rebates. For this six-month period, CMS reimburses at 106% of WAC.

Products are assigned a J-code for reimbursement purposes. It takes six to 21 months following launch to establish a J-code. Each individual J-code is reimbursed by CMS using either the AMP- or WAC-based calculation. However, CMS assigns a single J-code to all biosimilar versions of an original biologic product. As a result, the ASP for each biosimilar is a blended rate, taking into account the prices of different biosimilar versions.

Accordingly, for the first six months after biosimilar launch, CMS reimburses each individual biosimilar based on WAC. Biosimilar manufacturers may therefore be incentivized to launch at a higher WAC in order to maximize margin.

However, after six months, the blended ASP reimbursement calculation is applied instead. The blended rate does not incentivize the use of individual lower-cost biosimilars. In addition, the blended rate means there is a risk that a single player can sink overall ASP by offering significant discounts/rebates.

The Austrian Example

Austria operates a stepped-price system for generic medicines. Following the launch of biosimilar infliximab manufactured by Celltrion (Remsima, distributed by Astro Pharma, and Inflectra, distributed by Hospira), the medicine was classified as an generic and priced accordingly. As a result of this decision, the distributor opted not to apply for retail sector reimbursement in Austria – the treatment is available only through hospitals (accounting for 10.6% of pack sales).

Inappropriate incentivization also includes mandated pricing (see Box 5), or price caps relative to originator products. There are examples from the generics sector of where such caps have had unintended consequences (see Box 6).

Box 6: Generic Price Ceilings in Canada

In Canada, until relatively recently, generic medicine pricing for public drug plans was entirely devolved to the provincial and territorial level.

Provinces and territories chose to set generics prices relative to the prices of the original branded products. As a consequence, generics manufacturers naturally opted to set prices as close to this ceiling as possible, rather than seeking to compete on price in order to secure market share. Indeed, in Ontario, Quebec and other provinces, generics manufacturers paid "professional allowances" to pharmacists to secure shelf space, and thus increase market share.

As a result, numerous studies showed that Canada had some of the highest generics prices in the world. By benchmarking prices to the prices of the originator product, Canadian provinces ultimately hindered competition and Canadian payers missed out on significant savings. Belatedly, since 2013 the provinces have begun to explore different approaches to generics pricing. However, the most notable initiative, the pan-Canadian Competitive Value Price Initiative, still centers on benchmarking generics prices against originator prices – the major difference being that the Initiative applies across numerous provinces, and that the price ceiling (at 18%) has been set considerably lower than the former provincial-level ceilings.

Adequacy of Evidence Provided to Healthcare Professionals

The variety of policy approaches adopted by payers across the EU when it comes to biosimilar medicines is reflected in the patchwork provision of evidence to doctors to encourage them to prescribe these products. Overall, there is recognition that, across the continent, physicians are not fully aware of the regulatory pathways underlying biosimilar medicine approval nor are they given the necessary clinical evidence to support the prescribing of biosimilar medicines – either at the local or national level.

The lack of consistency in the provision of education can be attributed to a number of factors:

- The European Medicines Agency (EMA) and the European Commission (EC) have no role in relation to pharmaceutical pricing and reimbursement. These policies remain a national-level competence within the EU.
- Manufacturers could fill this gap, but are not always trusted by physicians.
- Regional and local payers have not always stepped in to provide physicians with the evidence they require.

It is unrealistic to expect physicians to do all of the heavy lifting when it comes to understanding the benefits offered by biosimilar medicines. Consequently, it is incumbent upon other key stakeholders – including regulators and payers, as well as manufacturers where appropriate – to support doctors by enabling them to access the correct information. Moreover, stakeholders need to do more to help doctors access unbiased information on biosimilar medicines (see Box 7).

To help physicians better understand the benefits offered by biosimilar medicines, stakeholders must rely on two key pillars:

- Education on the clinical benefits of biosimilar medicines
- Education on the health system benefits of using biosimilar products in the market

Educating Physicians on the Clinical Benefits

Patients and physicians need to be satisfied that biosimilar medicines offer a safe and efficacious alternative to original biologics. Across the literature, the importance of educating major decision makers including patients, payers and prescribing clinicians, is emphasized.

Patients, in particular, expect that their physicians will be able to explain to them that biosimilar medicines have no clinically meaningful differences to their originator biologic counterparts. Physicians, for their part, expect that key opinion leaders (KOLs), as well as payers (both local and regional, as well as national), pharmacists (and in particular hospital pharmacists) and regulatory authorities (national and at the EU level) will be able to supply them with the evidence to satisfy them that biosimilars are essentially the same as the original biologics. Manufacturers, meanwhile, must also play a role and work to build trust with other key stakeholders in the system.

According to an August 2015 report by Decision Resources' BioTrends Research Group,[11] for example:

- The majority of physicians surveyed in France, Germany and the United States indicated that they were at least moderately familiar with biosimilars.
- 50% of German respondents indicated that they are very or extremely familiar with biosimilars, compared with just 32% of French respondents and 34% of U.S. respondents.
- Reasons for these regional differences were likely to be cultural; France has historically been a brand-loyal market with few mechanisms to drive uptake of biosimilars or generics, evidenced by its low generic-penetration rate, whereas Germany has mechanisms such as prescribing targets that have driven high generic, as well as biosimilar, penetration.
- U.S. physicians' level of familiarity with biosimilars is likely driven by information published in peer-reviewed journals and medical conferences; although this information is also available to French physicians, U.S. respondents may choose to familiarize themselves with biosimilars to a greater extent owing to the possibility of substitution or step edits.

Such findings are important because, as noted by the Generics and Biosimilar Initiative (GaBI) journal:

Experience with biosimilars shows that physicians will be reluctant to prescribe them and patients reticent to use them if: (i) they lack trust in the science behind the safety and interchangeability evidence required by regulators, and (ii) the cost differences between the biosimilar and the reference listed product is too small. [12]

There is an urgent need to address the problems caused by the lack of trust that may be exhibited by physicians. This lack of trust functions on two levels. First, doctors may not trust the accuracy or veracity of the data behind the safety and efficacy evidence that is presented to them. Regulators, payers and manufacturers must therefore work to reassure physicians of the science that underpins the data.

Box 7: Educating on the Clinical Benefits

A number of recent studies have emphasised the importance of educating and informing stakeholders in relation to the clinical benefits offered by biosimilar medicines:

- Weise et al. (2012) note that: "A clear understanding of the scientific principles of the biosimilar concept and access to unbiased information on licensed biosimilars are important for physicians to make informed and appropriate treatment choices for their patients".[15]
- According to Rotensetin et al (2012), "patients will, at the very least, expect their HCPs [healthcare providers] to address their concerns that biosimilars are identical, and many may even want to review the data themselves [source: Shivers et al., 2012]".[16]

In addition, physicians may also distrust information that is provided to them by manufacturers. Among key stakeholders, it is clear that there is growing sense that manufacturers have specific interests that may not always align with the goals of payers, physicians and regulators. Thus, for example, there has been an upsurge in recent years of efforts to regulate the relationship between companies and healthcare professionals, with "Sunshine Acts"[13] in the UK, France and the U.S. among others. To counter this lack of trust, manufacturers must seek to adhere to Codes of Conduct set down by national industry associations. The risks of not doing so are evident. In October 2015, PharmaPhorum surveyed doctors in France, Spain and the UK and found that:

Less than 25 per cent of physicians currently report prescribing biosimilars and, while almost half have reported that they expect they will prescribe them in the future, the agents are only expected to account for up to 17 per cent of physicians' biologic patients over the next three years… The main reason that biosimilars are not prescribed is that many physicians continue to express concern over the efficacy and safety of these agents. They also feel there is a lack of clear guidance surrounding their use.

Moreover, PharmaPhorum notes that this is particularly the case among doctors in the UK. There are also, it notes, significant disparities in terms of the expected influence of local versus national guidance: "In Spain, local guidelines are expected to have the greatest impact on physicians prescribing biosimilars, whereas in France they [physicians] said they were more likely to be influenced by guidelines given at a national level. In Germany, almost a third of physicians (30 per cent) said they wouldn't be influenced by guidelines at all. This shows the disparity in attitude and behavior across markets."[14]

Thus, it is clear that stakeholders must focus on ensuring that physicians are given the necessary evidence to support their prescribing decisions, and that this evidence must be supplied by local, as well as national-level, EMA and other EU-level, stakeholders – a view supported by stakeholders cross a range of European markets (see Boxes 7 and 8). It is clear, too, that in some cases, healthcare stakeholders have continued to (inadvertently) signal that further evidence is needed to demonstrate the comparability of biosimilar medicines with original biologics. The approach of the Italian Society of Rheumatology, for example, suggests that biosimilar medicines should be subject to onerous comparability testing (see Box 8).

Box 8: Stakeholders Call for Improved Information on Biosimilars for Physicians

France:

Jean-Yves Le Déaut, member of the French parliament (Assemblée Nationale) for Meurthe-et-Moselle, addressed the French Senate (Sénat) Parliamentary Assessment Board on biosimilar medicines in May 2015,[17] stating that: "The key to success of acceptance by all biological drugs and their biosimilar is the confidence of all stakeholders: prescribers, pharmacists and patients. This confidence requires a major effort of information and training. The Ministry of Health is considering the establishment of a repository of biopharmaceuticals (reference or similar), with their indications and treatment precautions. Indeed, this idea could be very useful for all stakeholders."

Italy:

The Italian Society of Rheumatology stated in 2014 that "biosimilars should be limited to the indications for whom the "comparability test" was executed. Any claim must be validated with specific clinical trial, in particular for the extension of use of biosimilars inaxial spondyloarthritis, enteropathic or psoriatic arthritis, and, overall, pediatric patients. Validation should be conducted by direct comparison of the results coming from well-designed clinical trials on the innovative product and the original treatment. This would result in a great potential for the appropriate use of biological therapies in pediatric rheumatic diseases and enteropathic arthritis, in terms of management of the disease, and in terms of cost reduction."[18] In essence, the Society argues that its members would prescribe biosimilars more readily if more and better data were provided to them.

UK:

According to the British Society for Rheumatology, "both patients and healthcare professionals would benefit from more information about biosimilars, to allay concerns, encourage take-up and the adoption of good practice. The Department of Health, agencies such as NICE and MHRA, together with clinician and patient organizations should work with industry to facilitate this, through an awareness-raising campaign to empower patients to have an informed discussion with clinicians about the options available to them. Clinicians would benefit from having a better understanding of biosimilars from the efficacy and safety point of view and how they compare to the reference products."

Notably, the Society argues that "the introduction of new medicines, such as biosimilars, reinforces the need for a collaborative approach across primary, community and secondary care. There need to be clear lines of communication and information sharing across general practice, pharmacy and hospitals to ensure that all healthcare professionals along the pathway are aware of the medicines prescribed for a patient and any queries can be fed back promptly to the prescribing clinician. This would be supported by closer integration of information system across the whole pathway, through shared care records."[19]

Educating Physicians on the Health System Benefits

Physicians also need to be educated on the broader health system benefits offered by biosimilar medicines. Doctors need to trust that by driving the uptake of biosimilars, they are helping to deliver savings for the health system as a whole, and are helping to improve access for patients to much-needed treatments.

In Norway, physicians are educated in this way via the LIS tendering process (see Box 4). LIS functions as a forum through which physicians and key opinion leaders from each healthcare region can be brought together and be educated on the clinical and economic benefits of the medicinal products. The forum provides an objective, formalized process through which KOLs and physicians can challenge and interrogate the data and information supplied to them by stakeholders, including pharmaceutical manufacturers.

Through this process, physicians can develop an understanding of the systemic benefits, as well as the clinical benefits, offered by biosimilar medicines. Moreover, the process ensures that the general physician population trusts the information and guidance on biosimilars that emanates from LIS – removing the need for individual physicians to educate themselves on the benefits of these products.

Inconsistent Rules on Interchangeability

In Europe, countries have adopted a variety of approaches to the issue of interchangeability of biologic medicines with biosimilar versions. There has in the past been some confusion in the guidance supplied to physicians, and this variation persists.

As a result, country-specific rules on how physicians should approach the issue of biologic and biosimilar interchangeability are inconsistent. This means that physicians may be unsure when it is appropriate to switch certain patients (i.e. stable patients) who are already on treatment with a particular molecule, but may be suitable for a more cost-effective version of that molecule. For example in Denmark RADS have concluded that all originators and biosimilars are interchangeable unless proven not to be[21] whereas in Ireland a single switch is acceptable but multiple switches are not.[22]

Box 9: Education of Physicians[20]

According to the National Centre for Biotechnology Information (NCBI), physician education is one of the critical factors impacting "the integration of biosimilar medicines into oncology treatment paradigms and practices":

Clinicians will likely seek out practice guidelines and position statements from established scientific societies to help evaluate key information regarding biosimilars, such as efficacy, safety, comparability, and interchangeability with the reference biologic.

Variation in guidance across different markets and sometimes the type of guidance within the market makes it more difficult for physicians to educate themselves on the benefits of biosimilar medicines, and presents a potential risk to the realization of the potential of biosimilars.

Importantly, however, the five major EU markets leave the decision on when to switch patients in the hands of the physician.

Therefore, physicians need to be given the information they need to make the most appropriate decisions for their patients. If physicians are to be given the responsibility to assess when patients should begin treatment with a biosimilar medicine, then they must have confidence in the guidance offered by key opinion leaders.

Inconsistency in Messages from Manufacturers

Biologic manufacturers have also had a role to play in the lack of clarity surrounding the information about biosimilar medicines that is provided to stakeholders. The industry's message around biosimilar medicines has not always been helpful to policymakers.

To some extent, this lack of clarity is inevitable. It is to be expected that original biologic manufacturers with little stake in the biosimilars market would adopt a different position to those companies whose business is primarily geared toward biosimilar products. But even among originator manufacturers who have a significant stake in the biosimilars market, fundamental differences in core messages can be observed.

For example, manufacturers have adopted a variety of approaches to the issue of substitution. Some companies are in favor of permitting automatic pharmacy-level substitution of biologic medicines – but the majority of manufacturers emphasize instead the central role of physician choice, and argue against giving pharmacists the right to override physician prescriptions. Similarly, very few manufacturers in the biosimilars space favor the idea of requiring physicians to prescribe biologic medicines by international non-proprietary name (INN), only, but nonetheless there are some who do advocate this approach.

As a result of this diffusion, there has been no movement toward an agreed set of principles that could be shared with payers, physicians and patients.

Capturing the benefits of biosimilar medicines: a way forward

- A functioning competitive market is needed to deliver sustainability for payers, physicians and manufacturers alike
- Physicians, patients and payers require balanced and adequate education on the role that biosimilar medicines can play
- Payers need to ensure that physicians and manufacturers are properly incentivized to drive uptake of biosimilar products
- A focus by payers on acquisition cost rather than volume may appear attractive, but in the longer term will prove to be self-limiting, if not self-defeating
- For payers, sustainability means ensuring that longer-term opportunities for savings are preserved, by making the market attractive for manufacturers and maintaining incentives to invest in subsequent waves of biosimilar medicines
- For physicians, a sustainable biosimilars marketplace will enable consistently delivery of the best healthcare for patients, while retaining their freedom to prescribe
- For manufacturers, sustainability means incentives and opportunities to invest in new products, ensuring that trusted players remain in the market

Across the EU, governments are increasingly seeking ways in which to ensure that their healthcare systems deliver as much value to payers and patients as possible – and pharmaceuticals have been no exception to this drive for greater efficiency.

However, governments are also acutely conscious of the need to maintain patient access to vital treatments, and to ensure that their citizens can avail of the most innovative treatments for a range of conditions now coming on stream. The drive to control costs must be balanced against the need to maintain access.

Biosimilar medicines offer health systems across the continent the chance to square this circle. But to do this, governments must facilitate competition in the biologics space. Only a functioning competitive market can deliver the full potential of biosimilars.

Sustainability for Payers

There is, as we have seen, wide variation across the EU in terms of how governments and payers have chosen to address biosimilar medicines. Some have begun to implement policies that are conducive to developing competition in the marketplace – but others are lagging behind.

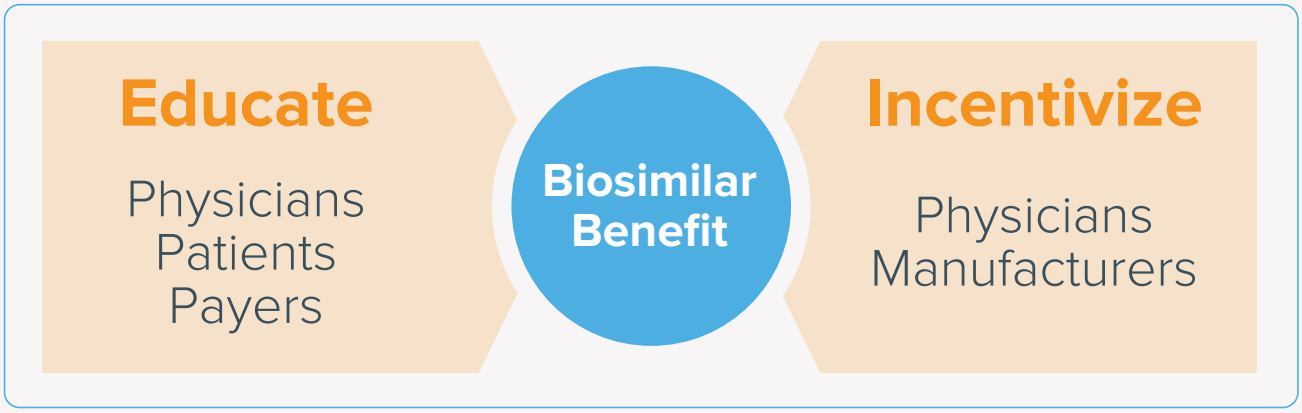
Above all, payers need to understand that biosimilar products offer a safe and efficacious alternative to original biologic medicines. Just as importantly, however, all stakeholders must understand that biosimilar medicines hold the key to enabling budget-holders to make budgets go further, while ensuring that patient access to these treatments is improved. As things stand, there is a risk that payers in some markets will not be able to realize this potential unless they take action.

Competition lies at the heart of the biosimilar value proposition, driving the virtuous circle and supporting the development of sustainable healthcare systems. Payers need to ensure that stakeholders are:

- Sufficiently educated on the benefits of biosimilars medicines
- Appropriately incentivised to invest in, and to use, biosimilar medicines (see Exhibit 12)

Currently, however, the situation across the EU is very heterogeneous, with varying levels of education and incentivisation among stakeholders.

Exhibit 12: Unlocking the Potential of Biosimilar Medicines



Source: IMS Health, IMS Consulting Group, Jan 2016

Education

To ensure that key stakeholders understand the benefits of biosimilars:

- **Payers** need to ensure that they are keeping themselves informed. The variation in policies adopted, as well as in biosimilar prices and uptake, across the EU, suggests that some payers do not understand the potential offered by biosimilar medicines.
- **Physicians** need to trust that biosimilar medicines offer a safe and efficacious alternative to original biologics. Moreover, they also need to be helped to understand the broader clinical and health system benefits of prescribing biosimilar products. To achieve this, payers need to be proactive in educating physicians about the benefits of biosimilar products. Doctors need more than an EMA approval to be fully comfortable prescribing these products, but equally may not trust manufacturers to educate impartially. It is unrealistic to expect individual doctors to educate themselves on issues such as interchangeability. Trusted stakeholders, including local regulators and payers, must therefore step in to ensure that physicians understand when, for example, it is appropriate to switch stable patients to treatment with a more cost-effective biosimilar. Given the inevitable heterogeneity associated with biologic medicines, the most appropriate approach is to leave the decision to individual, appropriately educated and incentivized, physicians.
- **Patients** are expected to accept new technologies, about which they may have only limited information. However, few patients are likely to be aware of the broader debate over biologic and biosimilar medicines. The key to bridging this gap lies in education. Payers need to reassure patients that biosimilar products are safe and efficacious – just as many health systems have done for generic versions of traditional small-molecule medicines.

Incentivization

In addition to education, payers need to ensure that stakeholders are properly encouraged to prescribe biosimilar medicines:

- **Physicians:** Payers need to ensure that doctors see a tangible benefit to prescribing biosimilar medicines. Physicians need to understand that prescribing biosimilar products delivers clinical benefits across the market as a whole, and that the cost-savings that result from biosimilar uptake enable more patients to access needed treatment.
- **Manufacturers:** Payers need to signal to manufacturers that they understand that pharmaceutical companies are profit-making entities that need to see medium and long term benefit in developing, marketing and selling biosimilar products. In practice, this means that payers need to make available volumes of patients for which they can compete, at sustainable prices.

Delivering on the Promise of Biosimilar Medicines

Biosimilar medicines help ensure health system sustainability by offering payers the opportunity to make savings that can be re-invested into the healthcare system, driving better access to treatments and improved outcomes for patients.

However, it is important for payers to understand how best to realize the potential on offer. A focus on acquisition cost rather than volume may appear attractive, but in the longer term will prove to be self-limiting, if not self-defeating.

Focusing on price risks ultimately constraining the longer-term opportunities for savings, by making the market less attractive for manufacturers, reducing incentives to invest in the development of subsequent waves of biosimilar products. By driving out competition, payers may lose out on the price-based savings they are seeking also. Furthermore, the focus on price and acquisition cost at the expense of volume risks stifling competition in the marketplace, reducing the level of physician choice and potentially limiting patient access to treatment.

By contrast, making patients available creates a market that is attractive to manufacturers, and fosters competition. Ensuring that physicians and patients have been appropriately educated enables doctors to trust in the benefits of biosimilars, and puts the choice in the hands of doctors and their patients.

Payers in some markets have begun to move toward an acceptance that facilitating competition, and providing appropriate education and incentives, is the best way to realize the full potential of biosimilar medicines. In other countries, much remains to be done.

Sustainability for Physicians

In a functioning competitive market, physicians and their patients are able to benefit from the improved choice on offer. This improved choice enables physicians to offer their patients the best treatments available, and to do so in a sustainable way.

For physicians, sustainability means:

- **Being able to consistently deliver the best healthcare for patients.** By prescribing biosimilar medicines, physicians can help ensure that more patients can be treated with the same medicines – and that scarce funds are freed up to treat patients with new medicines as they come on stream.
- **Maintaining their freedom to prescribe.** In a functioning competitive market, the power to prescribe resides with physicians, rather than payers or politicians. Doctors who are educated about the benefits of biosimilar products are best positioned to decide on the best treatment options for their patients.

Sustainability for Manufacturers

For manufacturers, a competitive marketplace helps to ensure the sustainability of their business and of their products in the market.

By making large volumes of patients available, for which manufacturers can compete, a functioning competitive market offers incentives for manufacturers to invest in new products. From a payer perspective, this is the best way to ensure that trusted players can remain in the market.

Most importantly, however, a competitive space, built around stability and predictability, gives manufacturers the confidence to invest beyond current biosimilar medicines and to look to the future wave of biosimilar products as more and more originators lose their exclusivity.

In so doing, a functioning competitive market enables payers, physicians and manufacturers to work together with patients to help ensure the sustainability of healthcare systems into the future.

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Murray Aitken is Executive Director, IMS Institute for Healthcare Informatics, which provides policy setters and decision makers in the global health sector with objective insights into healthcare dynamics. He assumed this role in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined

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About the Institute

The IMS Institute for Healthcare Informatics leverages collaborative relationships in the public and private sectors to strengthen the vital role of information in advancing healthcare globally. Its mission is to provide key policy setters and decision makers in the global health sector with unique and transformational insights into healthcare dynamics derived from granular analysis of information.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved patient care. With access to IMS Health's extensive global data assets and analytics, the Institute works in tandem with a broad set of healthcare stakeholders, including government agencies, academic institutions, the life sciences industry and payers, to drive a research agenda dedicated to addressing today's healthcare challenges.

By collaborating on research of common interest, it builds on a long-standing and extensive tradition of using IMS Health information and expertise to support the advancement of evidence-based healthcare around the world.

Research Agenda

The research agenda for the Institute centers on five areas considered vital to the advancement of healthcare globally:

The effective use of information by healthcare stakeholders globally to improve health outcomes, reduce costs and increase access to available treatments.

Optimizing the performance of medical care through better understanding of disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.

Understanding the future global role for biopharmaceuticals, the dynamics that shape the market and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.

Researching the role of innovation in health system products, processes and delivery systems, and the business and policy systems that drive innovation.

Informing and advancing the healthcare agendas in developing nations through information and analysis.

Guiding Principles

The Institute operates from a set of Guiding Principles:

The advancement of healthcare globally is a vital, continuous process.

Timely, high-quality and relevant information is critical to sound healthcare decision making.

Insights gained from information and analysis should be made widely available to healthcare stakeholders.

Effective use of information is often complex, requiring unique knowledge and expertise.

The ongoing innovation and reform in all aspects of healthcare require a dynamic approach to understanding the entire healthcare system.

Personal health information is confidential and patient privacy must be protected.

The private sector has a valuable role to play in collaborating with the public sector related to the use of healthcare data.

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