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PERSPECTIVE

A health economic guide to market access of biosimilars

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ABSTRACT

Introduction: Little is known about market access to biosimilars from a health economic perspective, except for studies that compute the budget impact of biosimilar use.

Areas covered: This comprehensive health economic guide to the market access of biosimilars focuses on the role of biosimilars in pharmaceutical innovation and competition, the objective of biopharmaceutical policy, the budget impact of biosimilars, and the cost-effectiveness of biologic therapy in the presence of biosimilars.

Expert opinion: We argue that the objective of biopharmaceutical policy in a health system should be to create a competitive and sustainable market for off-patent reference biologics, biosimilars, and next-generation biologics that makes biologic therapy available to patients at the lowest cost. Market access of biosimilars can contribute to this objective as a result of the lower price of biosimilars and price competition with alternative therapies. The resulting improvement in the cost-effectiveness of biologic therapy needs to be accounted for by revisiting reimbursement decisions and conditions. When examining the cost-effectiveness of biologic therapy following patent expiry, stakeholders need to consider residual uncertainties at the time of biosimilar marketing authorization, the nocebo effect, market entry of a second-generation reference biologic with a different administration form than the biosimilar, and value-added services.

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KEYWORDS
Biosimilar; budget impact; cost-effectiveness; market access

1. Introduction

There is room to improve patient access to biologic therapy. For instance, a multinational survey in Europe and Canada found that 19–24% of the dermatologists considered costs to present a hurdle to access biologic therapy in psoriasis [1]. Another survey showed that infliximab, etanercept, adalimumab, certolizumab pegol, golimumab, abatacept, tocilizumab, and rituximab were not reimbursed for rheumatoid arthritis in 22% of the European countries and that the cost of annual treatment with biologic therapy surpassed gross domestic product per capita in 57% of these countries [2]. Given that costs are one factor influencing access, the market entry of biosimilars, medicines which exhibit similar efficacy at a reduced price as the reference biologic and which can be launched following the expiry of patent and exclusivities of the reference biologic, is instrumental in supporting patient access to biologic therapy.

To date, market access of biosimilars has received little attention in the health economic literature, except for studies that have simulated or calculated the savings generated by using biosimilars instead of reference biologics [3]. The aim of this *Expert Opinion* article is to provide a comprehensive health economic guide to the market access of biosimilars. For this purpose, the article discusses: a) the role of biosimilars in pharmaceutical innovation and competition; b) the objective of biopharmaceutical policy; c) the budget impact of biosimilars; d) the impact of biosimilar entry on the cost-effectiveness and reimbursement of biologic therapy; and e) the factors affecting the cost-effectiveness of biologic therapy following patent expiry. This guide will help decision and policymakers to optimize the use of biosimilars in a market environment consisting of off-patent reference biologics, biosimilars, and new innovative chemical and biologic medicines.

We illustrate our arguments by drawing on published evidence related to Europe (and with a few additional examples from other countries). This geographical focus is chosen because there is more extensive experience with biosimilars in Europe than in less mature markets such as the United States (although the number of biosimilars entering the market in the United States is in line with that in Europe since 2017) or Canada [4]. Also, marketing authorization frameworks, pricing and reimbursement regulation, and biosimilar policies vary between countries [5,6]. Examples relate to a variety of products given that market dynamics differ between classes of biosimilars (and biologics) depending on, for example, product features, observability of effect, duration of clinical experience, and use in supportive or therapeutic care [7].

This *Expert Opinion* article is based on a scoping review, a method particularly suited to provide an overview of a recent area of research such as health economic aspects of market access of biosimilars. The literature search encompassed the peer-reviewed literature (PubMed and relevant

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Article highlights

- The objective of biopharmaceutical policy should be to create a competitive and sustainable market comprising off-patent reference biologics, biosimilars, and next-generation biologics that makes biologic therapy available to patients at the lowest cost.
- The cost of biologic therapy can be reduced by the market access of biosimilars and by price competition with alternative treatments.
- Budget impact analyses need to consider all relevant market dynamics, including the evolution in disease epidemiology, the initiation of biologic-naïve patients on biosimilar and switching practices for patients treated with a biologic, price competition with alternative therapies, and the market entry of new innovative chemical or biologic medicines.
- The improvement in the cost-effectiveness of biologic therapy in the presence of biosimilars needs to be accounted for by revisiting reimbursement decisions and conditions.
- When examining the cost-effectiveness of biologic therapy following patent expiry, stakeholders need to consider residual uncertainties at the time of biosimilar marketing authorization, the nocebo effect, market entry of a second-generation reference biologic with a different administration form than the biosimilar, and value-added services.

This box summarizes the key points contained in the article.

journals not indexed in PubMed such as the Generics and Biosimilars Initiative Journal) and the gray literature (abstracts of International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conferences, consultancy reports, policy documents, government agency, and company websites). The search terms included 'reference biologic,' 'biosimilar,' 'next-generation biologic,' 'off-patent,' 'budget impact,' 'savings,' 'affordability,' 'cost-effectiveness,' 'economic evaluation,' 'health technology assessment,' 'reimbursement,' 'competition,' 'innovation,' 'pharmaceutical policy,' 'substitution,' 'switch,' 'tender,' and 'gainsharing.' The bibliography of the included articles was searched for relevant references.

2. Competition versus innovation

It is often argued that biosimilar competition provides a disincentive for manufacturers to invest in research and development of new biologic therapies, i.e. market entry of biosimilars may threaten the economic viability of reference biologics as a result of possible price competition. On the other hand, it can also be argued that manufacturers may safeguard their economic viability by focusing on the development of new biologic therapies for which there is no biosimilar competition as long as patents and exclusivities have not expired. This can be illustrated by two examples. First, of the 14 manufacturers that had biosimilars in their portfolio out of the worldwide top 25 manufacturers based on prescription drug sales in 2015, all but one also developed reference biologics [8]. Second, following the patent expiry of Humira® (adalimumab, AbbVie), the world's best-selling medicine, and the market entry of adalimumab biosimilars, AbbVie chose to invest in the research and development of new biologic and chemical therapies (like JAK-inhibitors) [9].

Little research has been conducted on how biosimilars may have an influence on the dynamics of competition and innovation in the pharmaceutical sector from an industrial economic perspective. In this respect, for instance, a European study suggested that the market presence of at least two biosimilar manufacturers induce competition [10]. Using a theoretical model, a US study explored biosimilar market access and price evolution in the off-patent biologic market [11].

3. Biopharmaceutical policy and biosimilars

We believe that biopharmaceutical policy should aim to create a competitive and sustainable market for off-patent reference biologics, biosimilars, and next-generation biologics with a view to making biologic therapy available to patients at the lowest cost, rather than to promote biosimilar uptake. This serves to maximize savings from lower-priced biosimilars and from price competition with other biologics. Hence, the relevant outcome measure is the evolution in the average cost of biologic therapy over time instead of biosimilar market share. For instance, the observation that hospital expenditure (net of discounts) per patient fell by 44% for etanercept and by 50% for infliximab between 2014 and 2018 in the Netherlands is, in our opinion, a key indicator of a successful biosimilar policy [12]. Focusing on the class of erythropoiesis-stimulating agents (including off-patent reference biologics, biosimilars, and next-generation biologics), the volume-weighted average ex-manufacturer price per defined daily dose had fallen by 27% in European Union countries in 2018 as compared to the year before the first biosimilar epoetin product entered the market [4].

However, limited data are available about the evolution in the cost of biologic therapy over its life cycle. The Swedish Dental and Pharmaceutical Benefits Agency publishes each year a price comparison of outpatient medicines in 20 European countries in the years after market approval, which gives an idea of how costs change following patent expiry, taking into account the caveats that data relate to list prices and are not limited to biologic medicines [13].

Examples of biopharmaceutical policies that focus on making biologic therapy available to patients at the lowest cost are found in a number of European countries (see Table 1). Although the objective of biopharmaceutical policy should not be to promote biosimilar uptake as such, we acknowledge that a minimum biosimilar market share is likely to be one of the factors required to create a competitive market environment for biologic therapy. Policies affecting biosimilar uptake have been discussed elsewhere [14–17].

4. Budget impact of biosimilars

Due to their lower price, biosimilars provide savings to the pharmaceutical budget and support the sustainability of the health-care system. For instance, price comparison in EU countries showed that rituximab biosimilars were 39% less expensive than reference rituximab at the manufacturer level and

Table 1. Examples of policies that aim to make biologic therapy available to patients at the lowest cost.

Country	Biopharmaceutical policy
Austria	When multiple products are on the market, physicians are encouraged to prescribe the most cost-effective product [14]
Belgium	Policy is geared at promoting the use of a 'cheap' biologic medicine, be it a biosimilar medicine or the reference biologic with a reduced price [18]
Denmark	Amgros organizes national tenders for hospital medicines, selecting the cheapest product [19]
England	NHS England has set targets for the uptake of 'best-value biologics' in specialized services for both new and applicable existing patients [20]
Ireland	The Health Service Executive Medicines Management Programme identifies 'best-value biologics' based on 13 criteria (including cost), and Prescribing and Cost Guidance is published to support clinicians in prescribing these medicines [21]
Italy	If more than three biologic/biosimilar products using the same active substance are available, physicians need to prescribe one of the three cheapest products as identified in a regional tender (law 232/2016)
Slovakia	A reference-pricing system groups biologic and biosimilar medicines based on the same active substance and administration form, and sets the reference price at the level of the cheapest product [22]

86% cheaper at the retail level [23]. The lower price of biosimilars arises from reduced costs of researching, developing, and marketing biosimilars: R&D costs of a biosimilar have been estimated to amount to 100 USD – 300 USD million (as compared to 2.6 USD billion for an innovative medicine, including the cost of failures) [4,24,25].

In addition to the lower price of biosimilars, market entry of these products may induce competition and, thus, reduce the price of the reference biologic. A budget impact analysis quantified the relative contribution of biosimilar uptake and price competition to the overall savings of €153 million arising from the launch of rituximab biosimilars in Italy over 5 years [26]. This study found that price competition was the dominant driver and accounted for 67% of the savings. In the United Kingdom, the uptake of biosimilar infliximab generated 65% of the savings and price competition made up 35% of the savings from March 2015 until February 2017 [27]. Instead of relying on price competition, some countries regulate prices following biosimilar market entry: for example, the price of the reference biologic is required to drop (at least) to the level of the biosimilar price in Spain, although price competition can lead to further price reductions [28].

IQVIA used a modeling exercise to estimate biologic spending and savings from biosimilar competition as a proportion of total prescription medicine spending in 2019 [4]. In the case of Germany, where prices in the retail market are established through rebate contracts between health insurance funds and manufacturers, biologics accounted for 11% of the total prescription medicine spending, savings in list prices from actual biosimilar competition amounted to 2%, and additional savings of 6% could be attained if biosimilar competition is fully leveraged.

Savings arising from biosimilar uptake and price competition depend on, for example, the procurement mechanism. Tendering is such a mechanism, which is widespread across Europe, although the specific features tend to differ between countries [29]. Table 2 describes tender mechanisms in various countries and qualitatively assesses how the design features of these tenders influence the competition and sustainability of the market, the risk of shortages, and the physician freedom of product choice [30]. According to an IQVIA report, single-winner tenders at the hospital level may maximize price competition, but they exclude other manufacturers from the market, thus increasing supply risks and threatening long-term market sustainability [30]. The evidence also indicated that multiple-winner tenders may generate the largest savings because they attain price decreases on all tendered products for all uses/indications. Although the price is a key criterion for awarding tenders for biologics, it needs to be noted that criteria other than price can be taken into account (see Figure 1) [31].

Savings arising from biosimilar competition can be re-invested to treat more patients with the same disease or can be re-allocated to treat patients suffering from other diseases [35]. For instance, a UK study explored whether more health

Table 2. Qualitative assessment of tender mechanisms in European countries.

Country	Tender features	Enhances competition	Improves sustainability	Decreases risk of shortages	Guarantees physician freedom of choice
Belgium	Tenders per hospital or hospital group, usually one winner, variable duration [32]	+	+	-	--
Denmark	One-year national tender for hospital medicines with only the cheapest product being reimbursed [19]	++	−−	−−	−−
England	NHS England has tender design for adalimumab that splits up market in 11 hospital groups, provides access to reference product and biosimilar adalimumab, and grants market shares to multiple manufacturers depending on their price bids [33]	++	++	++	++
Norway	One-year national tender per indication with all products being reimbursed and ranked based on price, and recommendation to physicians to prescribe cheapest product [29]	++	-	-	-
Poland	One-year tenders per hospital with expectation that only the cheapest product is reimbursed [29]	+	--	-	--
Sweden	Regional tenders for hospital medicines, usually for 2 years (shorter duration when new competitors are expected), one winner or multiple winners (with all products being reimbursed and recommendation to physicians to prescribe cheapest product) [29,34]	+	+	+	+

Criterion	Key points
Market authorisation	• Licensed indications • In-country market authorisation (expected authorisation is sufficient in some countries)
Supply guarantee, logistics & support	• Locations of manufacture, packing and storage • Logistics arrangements (distribution and delivery) • Process for urgent deliveries • Customer support • Policy on returns/expired products
Ease of implementation	• Efficient use/handling • Dissolution rate (IV-product) • Device: Patient experience • Excipients & potential allergens (including animal sources used in production) • Latex-free packaging • Shelf life from date of manufacture • Stability pre-post-reconstitution and in/out of refrigeration
Presentation	• Technical specification (vial size, concentration, etc) • Product sample • Appearance of solution

Criterion	Key points
Packaging	• Photograph/mock-up • Robust primary packaging • Clear labelling on secondary packaging • Peel off labels / 2D barcode • Storage volume • Compliance with Falsified Medicines Directive (EU-only)
Clinical data	• Clinical studies (design, results) • European Public Assessment Report (EPAR) • Pharmacovigilance/post-marketing study plans • For SC-product: discomfort experience for patients
Manufacturer experience	• Track record of consistent quality production of biosimilars
Services to support implementation	• Services offered for HCP education, number of hours • Patient information (product-specific, no direct patient contact)
Policy and sustainability	• Company sustainability policy • Product-specific sustainability (manufacture & logistics) • Agreement to comply with (and ensure suppliers comply with) international labour laws, etc

Figure 1. Tender criteria for biologics other than price [31].

gain could be generated by using biosimilar adalimumab savings to treat additional patients suffering from rheumatoid arthritis or to treat patients with melanoma, hepatitis C, multiple sclerosis, Duchenne's disease, or non-small cell lung cancer [36]. As a result of the better cost-effectiveness of the available therapy for hepatitis C, a higher number of quality-adjusted life years were gained when biosimilar adalimumab savings were spent on treating patients with hepatitis C rather than on treating more patients with rheumatoid arthritis.

Savings may also serve to expand access to treatment in for example Eastern-European countries within the constraints of the same pharmaceutical budget [37]. In the Czech Republic, additional 1,000 patients with inflammatory bowel disease could be treated with biologic therapy in 2014 (as compared to 2013), thanks to savings from biosimilar competition [38]. However, this effect was not observed in Hungary following the market entry of biosimilar infliximab: most biologic-naïve patients who qualified for reimbursement in the indications of infliximab were initiated on treatment with other patented reference biologics and patients treated with reference infliximab were largely switched to other patented reference biologics [39]. This example emphasizes that the budget impact of biosimilars should not be investigated in isolation, but also needs to consider shifts in physician prescribing behavior.

It is often argued that savings from biosimilar competition provide 'headroom for innovation' and allow society to reimburse new innovative medicines [35]. As the amount of biosimilar savings may not suffice to cover all patients who are eligible for the new medicines, the overall pharmaceutical budget may actually increase. Nonetheless, we believe that such an increase is valuable if these new medicines are cost-effective.

Countries such as France, Germany, Norway, and the United Kingdom have set up gainsharing arrangements [10], so that savings from biosimilar competition flow back to stakeholders (such as health-care payers, hospitals, and physicians) and can be used to improve patient care. Savings can also cover the possible costs involved in non-medical switching, i.e. when a patient is switched from a reference biologic to its biosimilar, is switched back, or is switched between biosimilars out of an, for example, economic rationale [40]. Whether non-medical switching from reference biologics to biosimilars is associated with costs is not (yet) clear: a recent systematic literature review found limited evidence on this topic and pointed to methodological limitations of existing studies [41]. Nevertheless, NHS Scotland, for example, recommends to implement 'invest to save' arrangements to pay for managed switching programs now with a view to generate savings from biosimilar competition later [42].

Finally, budget impact analyses are typically carried out over a period of three to 5 years. From a methodological perspective, a budget impact analysis of a biosimilar needs to consider all relevant market dynamics during that time horizon, including the evolution in the epidemiology of the disease, the initiation of biologic-naïve patients on a biosimilar, and switching practices for patients treated with a biologic, price competition with alternative therapies, the market entry of new innovative chemical or biologic medicines (see Figure 2). For instance, a study calculated the budget impact of biosimilar infliximab in rheumatology and inflammatory bowel disease, taking into account the launch of vedolizumab, biosimilar etanercept, and biosimilar rituximab over the studied period [43]. However, few budget impact analyses of biosimilars to date have been able to capture the broad market environment in which biosimilars are used [3].

5. Economic evaluation of biosimilars

Given that a biosimilar provides similar efficacy and safety at a lower price than the reference biologic, biosimilar use improves the cost-effectiveness of biologic therapy. This can

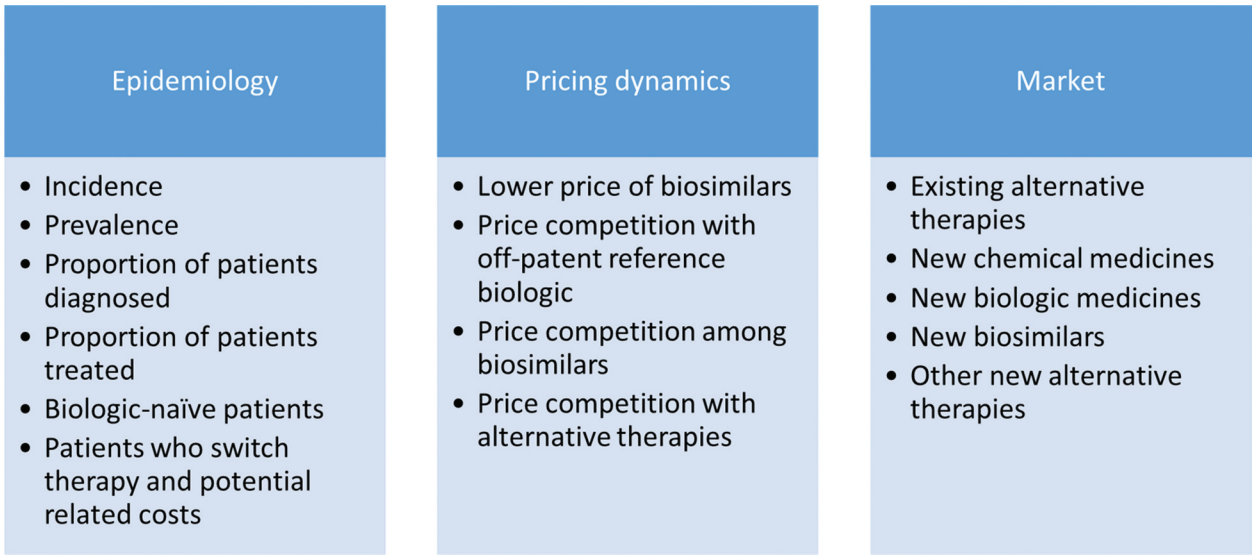

Figure 2. Elements of market dynamics to consider in budget impact analysis of a biosimilar.

be exemplified by a Canadian economic evaluation that calculated the cost-effectiveness of cetuximab plus best supportive care as compared to best supportive care for metastatic colon cancer: the incremental cost-effectiveness ratio was 299,613 USD per quality-adjusted life-year gained with reference cetuximab and 261,126 USD per quality-adjusted life-year gained with biosimilar cetuximab [44].

It follows that the cost-effectiveness of biologic therapy can change through its lifecycle as a result of, for example, the market entry of biosimilars or of new innovative chemical or biologic medicines. This also implies that new innovative medicines which charge a premium price may struggle to be cost-effective and receive reimbursement when the therapeutic arsenal includes biosimilars of an earlier generation of biologic therapy [45,46].

The improved cost-effectiveness of biologic therapy due to biosimilars may have an influence on reimbursement decision and on reimbursement conditions.

First, improved cost-effectiveness may allow to award reimbursement: for instance, the English National Institute for Health and Care Excellence (NICE) concluded in 2016 that infliximab treatment with only the cheapest product is recommended for adults suffering from severe active ankylosing spondylitis whose disease has not responded adequately to or who do not tolerate non-steroidal anti-inflammatory drugs [47].

Second, improved cost-effectiveness may allow to grant reimbursement in a sub-population: a US economic evaluation, for example, demonstrated that not only reference bevacizumab but also biosimilar bevacizumab (at a hypothetical 30% price reduction) was not a cost-effective add-on to first-line therapy for patients with advanced ovarian cancer [48]. However, biosimilar bevacizumab was cost-effective in patients with stage IV disease, in ECOG PS 1 patients, and in patients at a high risk of disease progression. What price reduction of biosimilar bevacizumab will be actually observed in the US market depends on a myriad of factors, including R&D costs, the extent of competition (and the number of biosimilar products entering the market), rebate contracting, and the occurrence of industry practices such as patent litigation activities and 'pay for delay' agreements [49].

Third, improved cost-effectiveness may allow to extend reimbursement to indications for which the reference biologic was not reimbursed: for instance, biosimilar epoetin alfa was fully reimbursed for the treatment of anemia, kidney failure, and cancer in Slovakia and Croatia in 2016, while reference epoetin alfa was not reimbursed for these indications [50]. Although reference somatropin is not reimbursed for the indication of short stature in children born too small for gestational age in Poland, biosimilar somatropin was awarded reimbursement for this indication following an assessment by the Agency for Health Technology Assessment and Tariff System (AOTMiT) in 2014 [51].

Fourth, improved cost-effectiveness due to biosimilars may contribute to the cost-effectiveness (and thus reimbursement) of combination treatments involving new innovative biologics. NICE, for example, found that the incremental cost-effectiveness ratio of the combination treatment consisting of pertuzumab, intravenous trastuzumab, and chemotherapy for HER2-positive early-stage breast cancer in adults who have lymph node-positive disease fell below the threshold value of £20,000 per quality-adjusted life-year, if the economic evaluation applied discounted prizes of pertuzumab and biosimilar trastuzumab [52].

Fifth, reimbursement conditions may change as a result of the improved cost-effectiveness of biologic therapy following the market entry of biosimilars, so that biologic therapy is reimbursed at an earlier stage of the disease or as an earlier treatment line or that physician prescribing restrictions are lifted [35]. For instance, a South Korean economic evaluation found that earlier use of biosimilar etanercept was cost-

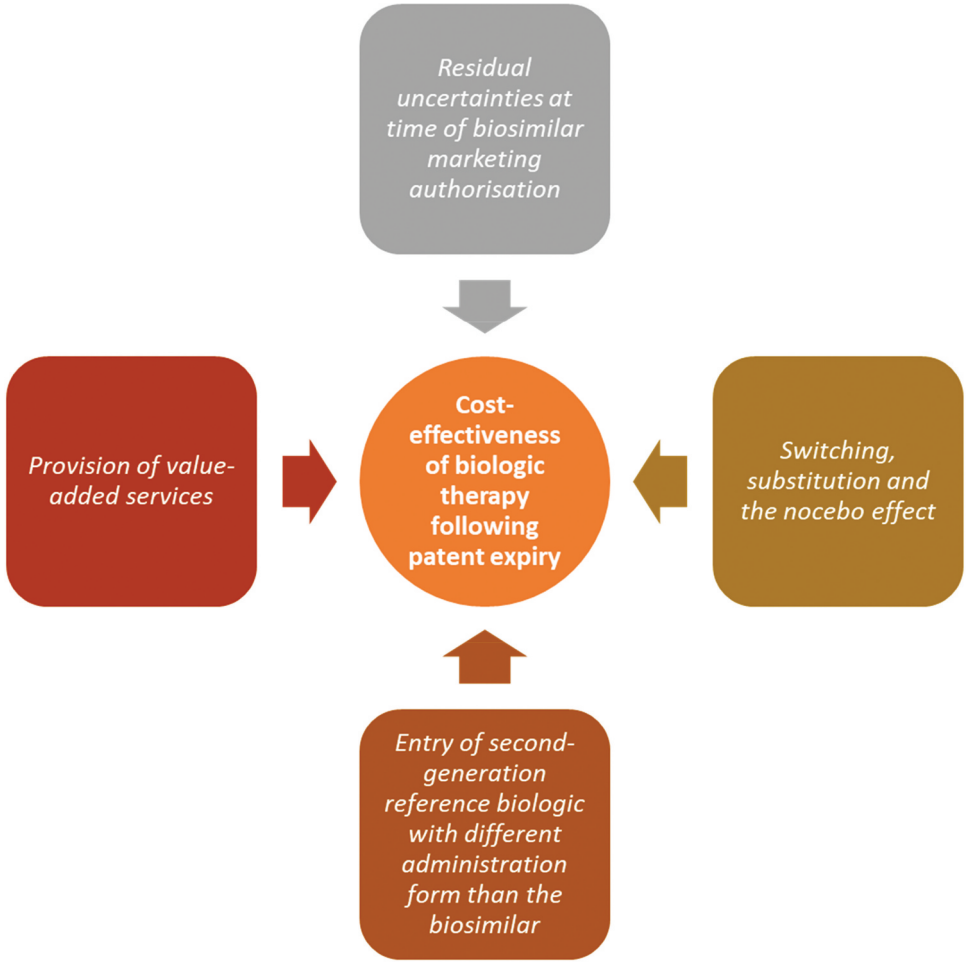

Figure 3. Factors influencing cost-effectiveness of biologic therapy following patent expiry.

effective in the treatment of rheumatoid arthritis following the failure of methotrexate therapy [53].

6. Factors influencing cost-effectiveness of biologic therapy following patent expiry

As indicated in Figure 3, we believe that several factors may influence the cost-effectiveness of biologic therapy following patent expiry.

A biosimilar receives marketing authorization based on the totality of the evidence, although residual uncertainties related to the benefit-risk assessment may remain at this stage (as is the case with any medicine), which can be addressed through post-marketing pharmacovigilance [54]. This can be illustrated by a UK economic evaluation of biosimilar infliximab for Crohn's disease, which explored the impact of a hypothetical difference in the immunogenetic profile of reference and biosimilar infliximab on cost-effectiveness [55]. The use of biosimilar infliximab was supported by the base case analysis given that both reference and biosimilar infliximab generated 0.803 quality-adjusted life-years over a one-year time horizon, but biosimilar infliximab (healthcare costs of £18,087) was less expensive than reference infliximab (£19,176). In the scenario tested in a sensitivity analysis that 50% of the patients would develop antibodies to biosimilar infliximab and 12.4% to reference infliximab, the minimum price reduction for biosimilar infliximab to remain the optimal treatment would need to be less than the actual price difference between reference and biosimilar infliximab. In the meantime, it was shown that this scenario is hypothetical, as a reference and biosimilar infliximab show an almost perfect cross-immunogenicity [56].

A second factor relates to the switch from a reference biologic to its biosimilar. In this respect, it should be noted that interchangeability is decided by each individual European Member State and that substitution practices vary between European countries. In the United States, a biosimilar can be designated interchangeable if it meets specific requirements and interchangeable products can be substituted in the pharmacy without physician consent [57]. Different switching and substitution practices may influence the cost-effectiveness (and the budget impact) of biologic therapy, especially in the context of the potential occurrence of the nocebo effect. This effect is not associated with the products involved, but relates to a patient's negative perception of the switch [58]. Therefore, we believe that there is a need for real-world economic evaluations that explore the cost and effectiveness implications of

switching from reference biologic to biosimilar medicines and account for a potential nocebo effect.

A market trend that we observe is the development of a second-generation reference biologic that has a different administration form than the first-generation reference biologic and its biosimilars: e.g. subcutaneous forms of reference trastuzumab and rituximab next to intravenous biosimilar trastuzumab and rituximab. The administration form has implications in terms of, for example, the health-care setting in which the biologic is used (hospital versus home), biologic preparation and administration resource use, dosing regimen (body-weighted adjusted dose versus fixed dose), use in combination with intravenous chemotherapy, health-care professional and patient convenience and preferences [59], all of which may have an impact on the overall costs and effectiveness of biologic therapy [60]. We now see a similar situation with the market entry of the subcutaneous form of reference vedolizumab for the treatment of inflammatory bowel disease (in response to the development of subcutaneous infliximab by Celltrion). To account for these implications, we argue that a full economic evaluation comparing a second-generation reference biologic and the first-generation biosimilar with a different administration form is required.

Some manufacturers offer value-added services in addition to the reference biologic or its biosimilar. Examples of such services that may provide value to payers, providers, physicians, and patients are disease programs that aim to support patient adherence, administration service, educational programs, and therapeutic drug monitoring [3,10,61]. As value-added services may influence the costs and effectiveness of biologic therapy, we believe that economic evaluation needs to assess a reference biologic or a biosimilar in combination with its value-added services.

7. Expert opinion

This *Expert Opinion* article has argued that the cost of biologic therapy can be reduced by the market access of biosimilars and by price competition with alternative treatments. The resulting improvement in the cost-effectiveness of biologic therapy should lead to a revision of the reimbursement decision and conditions. Budget impact analyses and economic evaluations need to compare all aspects of off-patent reference biologics, biosimilars, and new innovative chemical and biologic medicines, as these products influence the budget impact and cost-effectiveness of biologic therapy.

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Declaration of interest

S Simoens and A Vulto have founded the KU Leuven Fund on Market Analysis of Biologics and Biosimilars following Loss of Exclusivity (MABEL). S Simoens was involved in a stakeholder roundtable on biologics and biosimilars sponsored by Amgen, Pfizer, and MSD; he has participated in advisory board meetings for Pfizer and Amgen; he has contributed to studies on biologics and biosimilars for Hospira (together with A Vulto), Celltrion, Mundipharma, and Pfizer; and he had speaking engagements for Amgen, Celltrion, and Sandoz. S Simoens is a member of the leadership team of the ISPOR Special Interest Group on Biosimilars. A Vulto is involved in consulting, advisory work, and speaking engagements for a number of companies, a.o. AbbVie, Accord, Amgen, Biogen, Fresenius-Kabi, EGA (now Medicines for Europe), Pfizer/Hospira, Mundipharma, Roche, and Sandoz. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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