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Biosimilars for Healthcare Professionals

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Product naming, pricing, and market uptake of biosimilars

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With a number of patents on biological medicines soon to expire in the US, multiple stakeholders – from policymakers to manufacturers to payers – have been debating the structure of regulatory frameworks and in particular, naming conventions for biosimilars. A key area of concern has been the potential impact of naming, and specifically, whether distinguishable non-proprietary names for biosimilars will affect pricing and market uptake of biosimilars. One perspective asserts that because biosimilars are not identical to the originator biological, distinguishable names will allow for identification between biosimilars and originator biologicals. Alternatively, proponents of identical non-proprietary names argue that distinguishable names will hinder market uptake and subsequent consumer benefits. In this review, we analyse the issue of nomenclature in the US biosimilar market from multiple stakeholders' perspectives. We find that multiple factors, including financial incentives, beliefs and behaviours of key stakeholders drive both the entry of biosimilars into the market as well as the extent of its adoption.

Keywords: Biosimilar, market uptake, nomenclature, pricing, regulatory issues, specialty pharmaceuticals

Introduction

The US Food and Drug Administration (FDA) recently approved the first biosimilar in the US – the first of an influx of biosimilars expected for the pharmaceuticals market as a result of a number of biological medicines reaching patent expiration in the US [1-3]. The first approval granted was for a recombinant colony-stimulating factor which is the biosimilar version of Amgen's filgrastim, marketed as Neupogen®. In particular, the FDA has given the biosimilar, made by Sandoz/Novartis, the interim name of filgrastim-sndz; thus, initially the FDA has decided on different non-proprietary names. More approvals are expected and as a result, many stakeholders are debating the regulatory frameworks around the introduction of biosimilars, including naming conventions for biosimilars. In particular, there is considerable controversy and debate around the use of identical versus distinguishable non-proprietary names between biosimilars and the reference biologicals.

A major issue is whether distinguishable non-proprietary names for biosimilars will affect market uptake of biosimilars [4]. One perspective asserts that because biosimilars are not identical to the originator biological, distinguishable names will allow for identification between biosimilars and originator biologicals [4]. It is argued that this will enhance traceability and pharmacovigilance thereby facilitating market uptake. Alternatively, proponents of identical non-proprietary names argue that distinguishable names will hinder market uptake and subsequent consumer benefits [5]. This school of thought argues that identical non-proprietary names would minimize the cost of processing claims and potential confusion arising from the use of prefixes and suffixes to distinguish therapies. Another perspective is that the role of non-proprietary product names is less relevant in the marketing and sale of biological medicines. As we explain below, this is because of the highly technical nature of the products, product distribution channels,

prescriber product familiarity, and the role of insurance in driving usage.

To help clarify and suggest a resolution on this debate, this paper examines the issue of naming from a multi-stakeholder perspective, and suggests that naming, by itself, will not affect market uptake. We describe how the biosimilar market in the US is likely to evolve, and provide analysis on the effect, if any, biosimilar nomenclature may have on pricing and ultimately market uptake. Using a targeted literature review, our analysis draws primarily from biosimilar entry and uptake in the European Union (EU), Australia, and Japan [6]. In doing so, we consider the impact of healthcare regulations, reimbursement and pricing schemes, provider preferences, and consumer behaviours on the biosimilars market. We also consider aspects of the introduction of generics in the traditional chemical drug market in the US, noting similarities and differences between generics and biosimilars.

Biotechnology innovations have enabled the development of a number of biological medicines [6]. By law, a biosimilar is required to be *highly similar* to an originator biological, which is also known as the reference product [7]. The FDA states that, '[a] biosimilar is a biological product that is highly similar to a US-licensed reference biological product notwithstanding minor differences in clinically inactive components, and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product' [8]. To qualify as biosimilar a drug must have the same mechanism of action, dosage form and strength, and prescribed use as the reference product [9]. An important distinction between biosimilars and their small-molecule counterparts, generics, is that biosimilars are not necessarily therapeutically equivalent to the reference product. In contrast to therapeutically equivalent generic drugs that must

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have chemically identical active ingredients as their reference drugs, biologicals are manufactured using living systems resulting in variations in the active substance between and within manufacturers [6]. Accordingly, the US Affordable Care Act (ACA) requires the FDA to make several key decisions about biologicals and biosimilars. This includes clinical trials investigation requirements, guidelines for biosimilar market entry, and the development of a naming policy [10].

There exists no uniform global definition for biosimilars. Countries around the world have enacted various regulatory requirements about what constitutes a 'biosimilar'. For example, the EU has guidelines requiring evidence (clinical trials and studies) to demonstrate that a biosimilar is highly similar in quality characteristics and biological activity to the reference product, with comparable efficacy and safety [6]. However, countries with less stringent regulations have classified a drug as a biosimilar when it might not receive approval under the EU guidelines because biosimilars are developed and commercialized for domestic patients at lower cost levels [11]. For example, in South Korea, biosimilar guidelines implemented in 2009 allow for the extrapolation and exemption of Korean biosimilar products from phase II clinical trials [11]. In March 2015, China issued final guidelines on biosimilars which mirrors that seen in the EU and US [11, 12]. Here, we define biosimilars as those products that would meet regulatory requirements in the US, EU, Canada, Japan, or Australia [13].

In 2010, the US Congress enacted the Biologic Price Competition and Innovation Act (BPCIA) in order to increase competition in the biologicals market [9]. The BPCIA was developed to provide a novel regulatory pathway for the approval of biosimilars balancing the protection of innovation of new biologicals by providing 12 years of market exclusivity, with encouraging future access to these high cost drugs by allowing entrants to compete after exclusivity and patent expiration. However, the BPCIA left the FDA to determine how non-proprietary names should be assigned to biosimilars.

Action by the FDA is particularly salient because many high-revenue biologicals marketed in the US have or are scheduled to come off patent in the near future, providing manufacturers the opportunity and incentive for biosimilar entry [14]. Now that the FDA is evaluating the first biosimilar applications, it is imperative to consider what factors are most likely to affect uptake in the US. Given the current debate around nomenclature and its impact on the development of the US biosimilars market, will product naming affect pricing and market uptake of biosimilar medicines?

Methods

To address its potential impact, we conducted a targeted literature review using PubMed and Google Scholar to examine the development of the biosimilar medicines market and the impact of product naming, if any, in the EU, Australia, and Japan, with a specific focus on the varieties of naming. Search parameters included 'biosimilar' OR 'subsequent entry biologic' OR 'follow-on biologic' AND 'regulatory pathway' OR 'regulations' OR 'approval' OR 'uptake' OR 'market entry' OR 'naming'. Internet searches using Google web search were also conducted to identify industry publications, recent press

releases, news items, and various regulatory guidelines related to biosimilars.

We assessed the impact of naming from four key stakeholder perspectives and the factors that drive each perspective. These were: from the perspective of 1) manufacturers; 2) patients; 3) providers; and 4) payers. In practice, these stakeholders are highly interconnected; however, addressing each position separately allows for a clearer analysis of incentives, constraints, and beliefs within each realm. An additional facet in the current debate on biosimilar naming centres on the role of distinguishable names in the pharmacovigilance system. For example, with manufacturers we focus on key areas of deviation between the regulations established for biosimilars versus generics. With respect to patients, we analyse patient perspectives in the small-molecules market and describe how patient acceptance influenced market uptake. For providers, we discuss the recent interest in Accountable Care Organizations (ACOs) and bundled payments, specifically describing how the growth of ACOs in the US may affect the uptake of biosimilars. Finally, we evaluate the pricing and reimbursement systems in the US in order to illustrate the ways in which payers can affect market uptake, with a particular focus on the Medicare system.

Results

While in the US, the FDA is developing regulatory guidelines for a biosimilar pathway; other countries have already forged a path from which lessons may be drawn. In particular, the EU, Japan, and Australia already have experience with biosimilar licensing, market launches, and competition. We provide a detailed overview of biosimilar uptake and the impact of nomenclature from key perspectives in the EU (examining Germany and Norway as cases of special interest representing more advanced markets in the EU), Australia and Japan.

European Union experience

The EU has permitted the entry of competitive biosimilars which generally (but not always) share the non-proprietary names of their reference products since 2005 [15]. While the approval of biological products for marketing within the EU is under the oversight of the European Medicines Agency (EMA), each EU country has a unique reimbursement system with different incentives in place for the use of biosimilars. One study estimates that between 2007 to 2020, biosimilars will have saved between Euros 11.8 billion and Euros 33.4 billion in eight EU countries [16]. The median retail price reduction as a result of biosimilar competition from 2006 to 2013 was 35% [17].

In each EU country, a government agency determines whether a biological will be included on the country's formulary and in the reimbursement system. The government agency may negotiate a biosimilar price that is 25% less than the reference price [18]. However, despite a policy of shared non-proprietary names, the market structures have been such that often the consumer or physician had little financial incentive to choose the lowest-priced biosimilar [6].

Throughout Europe, there is generally little financial incentive for the patient, the physician or the pharmacists to opt for the less expensive biosimilar product, with some exceptions, for example, Germany [19, 20]. Market shares of biosimilars vary

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considerably by product and country in the EU with those countries that have the highest market shares having the greatest incentives to use low cost products. While sales of biosimilars have been growing in the EU, the unintended consequences of some reimbursement systems have resulted in incentives that deter biosimilar competition, despite a shared names policy [6]. Some EU countries have set biosimilar prices at a fixed percentage below the price of the reference biological. These mandatory discounts of 30% in Spain [18], at least 20% in Italy, 40–70% in Austria, and 15% in France can deter competition [21]. Specifically, theoretically if a manufacturer of an originator biological decreases its price below the cost of producing the biosimilar, then the biosimilar will leave or not even enter the market. While such price competition might reduce prices in the short run, the long-run entry deterrence leads to increased prices.

Another example is Ireland's hospital level tendering, which resulted in perverse incentives for hospitals. Hospitals actually [22] chose the highest price biological, since 'the absolute size of the discount was largest and was retained by the hospital.' That is, the tendering system caused hospitals to have the most financial gain when choosing the highest priced drug. However, tendering generally leads to lower prices. For example, in England, each hospital has a budget and the ability to purchase biologicals with a competitive tendering process; if a biosimilar product is the lowest in price, the hospital is incentivized to purchase the biosimilar and use the saved resources elsewhere [22]. As a result, biosimilars constituted 80% of granulocyte colony-stimulating factor (G-CSF) sales and the UK physicians moved G-CSF back to first-line treatment due to the lower costs of the treatment. The UK's National Institute for Clinical Excellence has examined the seven human growth hormones that have been approved in the UK (including the biosimilar somatropin) and found no difference in clinical effectiveness. This suggests that in the case of human growth hormones utilization of the lower price drug has not led to losses in quality [22].

Some countries in the EU have therefore begun to restructure incentives. Several methods have been used to financially incentivize stakeholders to utilize lower priced biosimilars, leading to increases in biosimilars uptake. For example, the tendering system provides a clear example where the financial incentives resulting from the market, and not the naming of drugs, drive biosimilar uptake. Under national tendering, for a given duration of time, either all patients in that country or only new patients will receive the product of the manufacturer who wins the tender. In a national tendering system, the government will only pay for tendered product on its formulary, leaving prescribers effectively no choice.

The example of infliximab in Norway demonstrates how national tendering may decrease prices. In 2014, the Norwegian Medical Agency published the hospital tender price for the infliximab biosimilar. Inflectra® was offered at a 33% discount whereas Remsima® offered a 39% discount over the reference product [23]. Inflectra® and Remsima® are actually the same product produced by Cellitron, but Inflectra® is marketed by Hospira while Remsima® is distributed by Orion Pharma. In this case, Remsima® was chosen because it provided the government the lowest priced product. In 2015, the discount was increased to 72% [24]. Also, Norway is conducting a study for Remsima® to

determine if switching from originator (Remicade®) to biosimilar (Remsima®) is safe [25].

Germany has been successful in the uptake of biosimilars, and therefore provides an informative example regarding the factors promoting biosimilar uptake. For example, according to IMS in 2013, biosimilars had 53% of the epoetin and 51% of the G-CSF market in Germany [26]. In general, the German Government has encouraged the use of biosimilars, and provides an incentive system that does so [16]. Germany has a reference pricing system as well as biosimilar quotas for both regional sickness funds and physicians, and a rebate system. Biosimilar manufacturers also enjoy strong reputations with healthcare providers all of which result in stronger incentives for stakeholders to use low cost pharmaceuticals. Under reference pricing, physicians must inform patients that they must pay out-of-pocket the difference between the price of the drug chosen and the reference price. For drugs, patients pay 10% of pharmacy retail price with a minimum charge of Euros 5 and a maximum charge of Euros 10, a maximum of 2% gross income and difference from the reference price [16]. Since 1998, 'regional budgets replaced physician budgets based on practice specific prescription targets' [16]. If over budget by more than 15%, physicians receive a written notice asking them to reconsider their prescribing practices. If physicians exceed 125% of their budget they need to repay the amount above 115% unless this can be justified [16]. Accordingly, generics increased from 57% of prescriptions in 1994 to 76% in 2008 [16]. In Germany, the large insurance companies (sickness funds) use capitation payment and therefore create and run drug formularies [16]. 'These organizations negotiate for discounts and may choose the biosimilar to be on the formulary' [27]. Additionally, Germany's Federal Healthcare Committee has encouraged the use of biosimilars and is able to bargain for rebates. Sandoz, for example, in 2007 increased its Binocrit® discount from 15% to 33%, and obtained 30% of the market [26].

In Europe, government agencies often individually determine whether a biological will be included on the country's formulary and in the reimbursement system. This is also the case in Australia and Japan. However, in contrast to Europe, Australia and Japan have policies requiring unique qualifier codes following the non-proprietary name for most biosimilar products. For example, in Japan the biosimilars use non-proprietary name of reference product plus biosimilar and a number that indicates the order that the biosimilar was approved, e.g. a designator of '3' indicating the third biosimilar [15, 28].

Australia experience

The Australian Government adopted a biosimilar approval pathway in 2008, based on the existing system developed in the EU. In Australia, the Therapeutic Goods Administration (TGA) evaluates and licenses drugs, which then are evaluated according to the Pharmaceutical Benefits Scheme (PBS) [29]. Australia had originally planned to establish a naming system in which non-proprietary names for biosimilars include a prefix 'sim(a)' and a three-letter code for each biosimilar to distinguish the biosimilar from the reference drug [29–32]. However, in January 2015, the TGA announced that it is currently undertaking a review of its naming policy [33].

Under the Australian system, biological drugs are primarily administered in hospitals and more recently in community pharmacies. As in some countries in Europe, Australian hospitals may practice tendering and receive discounted prices from bulk orders, but will be reimbursed by PBS at the original price [29]. Thus, hospitals-based tendering puts downward pressure on drug prices and shapes the choices of its prescribers and patients.

Japan experience

Japan requires distinguishable non-proprietary names for biosimilars using qualifier codes [28]. For most biologicals in Japan, both the reference biological and the biosimilar non-proprietary name must bear a suffix to the non-proprietary name to distinguish the product. In the case of most biosimilars, the suffix also specifies that it is a biosimilar, the exception to this rule is for somatropin, or human growth hormone [28]. There has been a formal approval process for biosimilars in Japan since 2009, however, the government does not provide incentives to use biosimilars [34]. The government sets biosimilar reimbursement at 70–80% of the originator's price [35] and Japan does not allow interchangeability, substitution, or switching mid-treatment to a biosimilar [36]. Overall, uptake for biosimilars in Japan was estimated to be 6% in 2011, although the uptake for the epoetin alpha biosimilar was estimated at 25% in its first year [34]. A total of six biosimilars have received approval in Japan as of July 2014 [37].

Finally, while biosimilar competition in these three markets has fostered lower prices, price differentials between reference products and biosimilars in the EU have been smaller than in the small molecules market [6]. In particular, the median price retail reduction as a result of biosimilar competition from 2006 to 2013 was 35% [17].

The US experience

One of the main drivers of the BPCIA is to increase competition in the biologicals market and to control healthcare costs [9]. In particular, policymakers seeking fiscal restraint have advocated for biosimilars in order to control healthcare expenditures. Thirty years ago, the US was faced with similar concerns as it developed a framework for generic chemical drug entry. The resulting Hatch-Waxman Act was intended to balance competition and innovation, and has helped generic drugs generate over a trillion dollars in healthcare cost savings between 2002 and 2011 [38]. A similar trajectory is anticipated for biosimilars. A recent RAND study predicts that over the next decade biosimilar drugs in the US may lead to US\$44.2 billion in savings related to direct spending on biological drugs [39]. The targeted literature review revealed four US key stakeholder perspectives that are presented here.

Manufacturers' perspective

First mover disadvantage

In many markets the first entrant gains considerable advantage. However, this may not be the case for biosimilars due to greater uncertainty for the first entrant. For instance, in addition to the uncertainty regarding regulatory frameworks in nascent biosimilar markets, the first mover may face various legal costs as a result of patent litigation concerning the reference product. Similarly, the risks for the first mover to apply for interchangeability status may be large relative to the potential benefits.

Interchangeability and automatic substitution

The use of identical non-proprietary names does not indicate interchangeability, although may be perceived as doing so. According to the FDA, '[a]n "interchangeable" biological product is biosimilar to the reference product, and can be expected to produce the same clinical result as the reference product in any given patient. In addition, to be deemed an interchangeable biological product, it must be shown that for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch' [8].

Interchangeability may not be allowed until the biosimilar has a track record and has been demonstrated (through post-marketing studies) to produce results identical to that of the branded product. It is uncertain as to how long this process might take, if it ever occurs. In addition to the costs and uncertainty in how long it would take to achieve an interchangeability rating from the FDA, manufacturers must carefully consider the implications of applying for interchangeability and subsequently not achieving it.

The primary benefit of being the first interchangeable biosimilar in the US derives from one-year interchangeability market exclusivity accorded to the first interchangeable biosimilar. This exclusivity period is not granted to a biosimilar that is not interchangeable. If a drug can be the first biosimilar and also be interchangeable, it may only foreclose other interchangeable (not non-interchangeable) biosimilars from the market. This has very different implications from the exclusivity granted to small molecule generics. Specifically, an abbreviated new drug application (ANDA) grants market exclusivity for 180-days to the first generic drug for a given originator product. Thus, in the case of small molecules, the first approved generic drug is deemed the sole supplier of the generic for the branded drug product for 180 days and thus has more control over price until other competitors are permitted to enter the market. In this time period, the generic drug can generate substantial profits [40].

In the case of interchangeable biosimilars, it is likely that a few non-interchangeable biosimilars may already be approved and in the market. Thus, the interchangeable biosimilar may be competing against not only the reference product but also other biosimilars. The primary advantage of being interchangeable is that the therapy may become automatically substitutable at the pharmacy level, pending state law requirements. However, since most biologicals are administered by healthcare providers, such substitutability at the pharmacy level may not be important for a given product. Further, the costs associated with proving interchangeability are non-trivial [41]. Nonetheless, some sponsors developing biosimilars may seek an interchangeability designation as a differentiator for payers who may then grant more favourable formulary status to the interchangeable product. Such a formulary placement would favour the interchangeable product irrespective of the non-proprietary name.

Thus, the reduced benefit to manufacturers granted through interchangeability compared to the small molecule market suggests that interchangeability may be sought by few manufacturers and

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may not play a large role in promoting biosimilar entry. On the other hand, there is notable concern that physicians may perceive shared non-proprietary names to imply safe interchangeability between drugs [4]. In a 2012 survey of US physicians, 67% of respondents assumed that shared non-proprietary names implied it was safe for a patient to be switched between products when prescribing [42]. While below we describe why the decision to prescribe either a biosimilar versus the originator product may be driven by clinical and financial incentives instead of nomenclature, this lack of physician understanding suggests that physicians are indifferent to products, and shared non-proprietary names could lead to medically inappropriate switching.

In the EU, the substitutability between biologicals must be decided by each country [6]. However, based on the existing literature for markets where payers have more influence over prescribing practices (as is the case in the US) the issue of uptake will likely be around price negotiations – with the lowest price products likely to gain sales. Costly risks such as these may likely play a primary role in determining entry and dominate any effect that a naming policy may have.

In addition, there remains some confusion around what a biosimilar is and its relationship to its reference product. Recent physician surveys demonstrate that this confusion persists in the EU, where biosimilars have been approved since 2006 and share non-proprietary names with reference products [43]. The first biosimilar sponsor for each reference product market may likely need to invest resources educating stakeholders to achieve sufficient market utilization.

Competitive response

In the small molecules market, an overall lack of price responsiveness from originator product makers led them to lose over 80% of the overall market in a few months [44]. In contrast, biological reference product manufacturers have responded in myriad ways to the potential entry of biosimilars. The considerable competitive response from originator biologicals in the EU includes lowered prices, development of second generation biologicals by the originator, patent extension, and reduced frequency of dosages [45, 46].

In the US, patent defenses will likely play a role in determining market share. Also, companies that manufacture originator drugs are seeking to expand and improve all aspects of product formulations, dosing and perceptions over biosimilar competitors [22]. Given these dynamics, one would expect that, irrespective of naming policy, biosimilars will not achieve the same percentage of market share as generics even after the market has developed. Given the high costs of development and manufacturing, prices are unlikely to decrease by 80% or 90%, as was observed in the generics market. Prior to 2014, reductions ranged from 20% to 30% [39]. However, the recent discount of 72% observed in Norway may change this scenario and lead to larger discounts.

Patients' perspective

Consumer uptake of biosimilars will depend on both perceptions of safety and quality as well as price incentives. Presently, 84% of the total US small molecules chemical market consists of generic drugs, but this market share was only achieved over a

long time [46]. It took time for US consumers to accept generics despite the fact that they share a non-proprietary name with the reference product. Although having both shared names and bio-equivalence, today, patients still perceive differences between reference products and generics, and believe that in particular, brand-name drugs are more effective and safer than generics [47]. In the case of generics, shared non-proprietary names have not resolved consumer perceptions around whether drugs are identical; yet the market for generics remains substantial because generics are priced lower [48]. Notably, third-party payers have induced patients to use generics in a number of ways, including higher copays and excluding the branded product from their formulary and forcing consumers to pay full price for a non-formulary branded product [49].

Providers' perspective

In the US, there has been a heightened interest in ACOs and the use of alternative payment systems, such as fixed bundled payment systems to providers that would cover a group of products and services for a given diagnosis. To reduce healthcare costs while still delivering quality care [50-52]. Bundling will give physicians the incentive to prescribe the lowest cost and effective alternative in a given indication, whether a reference biological or a biosimilar, regardless of name. As long as physicians believe that the reference product and the biosimilar are truly similar, they will likely choose the lowest price product; as has been the case in Germany, a country with relatively high penetration of biosimilars [20].

In the US, tier pricing with higher copays for patients or percentage of cost, or reference pricing may be utilized [53]. Under reference pricing, the consumer is incentivized to take the lower priced biological, since they are paying out-of-pocket for the difference between the price of the drug they choose and the reference price. This may influence physician's prescribing patterns, particularly if patients question the higher price of a biological. Thus, under such a payment system, physician and patient incentives may be aligned and driven by reimbursement policies more than naming.

Payers' perspective

Our analysis of regions where biosimilars have already been introduced, combined with a review of the introduction of generics into the small molecules market in the US, reveals that financial incentives created by these systems, particularly through pricing, will determine the development of the biosimilar market, with little or no effect from naming. While in the US, the FDA is developing regulatory guidelines for a biosimilar pathway; other countries have already forged a path from which lessons may be drawn. While there is some evidence that biosimilar competition in other countries has fostered lower prices, price differentials between reference products and biosimilars in the EU have been smaller than in the small-molecules market [6, 16, 17, 54].

As market share of biologicals increases in the US, they may come under greater scrutiny from payers, due to high cost and efficacy questions, leading to an increasingly difficult market landscape for manufacturers. The mean annual cost of an originator biological is estimated to be US\$34,550, and some payers require co-insurance rates of up to 35% [39]. Moreover, the rate

of price increases for biologicals far exceeds the overall rate of inflation. Pricing suggests that in the US, the reimbursement system, and not naming, will greatly influence the development of the biosimilar market.

While the US reimbursement system is more complex than the EU, with both large private and public payers, financial incentives will still drive the biosimilar market. Reimbursement will develop similarly to the generic drug reimbursement system with one exception being that the reference product will likely compete in pricing. Manufacturers face risks when entering the market because they may have to compete for preferred formulary placement. Thus, third-party payers will have the ability to negotiate the best deal for their clients and may specify different copays for biologicals and biosimilars under a tier system. As in the US generics market, the tier system and copays will likely drive choice in the biosimilars market, with naming of little impact in market uptake.

Medicare spends billions of dollars on biologicals each year with expenditures expected to increase annually [55, 56]. The Medicare payment system is therefore a key driver in uptake. For Part B practitioner-administered biosimilars, Medicare reimburses each biological or biosimilar at its own 'average sales price' (ASP) (an amount set by the government based on pricing information submitted by manufacturers) plus 6% of the reference product's ASP. As a result, physicians receive, on average, the same monetary reward for both the reference product and biosimilars. Congress devised such a policy so that on average, physicians do not have a monetary incentive to prescribe the higher-priced originator product [55, 56].

As with ACOs, Congress is investigating ways to reduce Medicare spending. In particular, a bundling policy might encourage use of biosimilars [57]. Since Part B covers practitioner-administered drugs, bundling could potentially be easily adapted to include practitioner-administered drugs in order to encourage physicians to use biosimilars [57].

In a recent report to Congress [57], MedPAC evaluated three pricing strategies for Part B drugs that use information concerning a drug's clinical effectiveness to improve the value of Medicare spending. These strategies are: a) reference pricing; b) payment for results; and c) bundling. As mentioned previously, under reference pricing, the new drug must show better results to be priced above currently available products. Payment for results-based pricing ties the payment to the patient's outcome through a risk-sharing arrangement with the drug company. Medicare also has the option to bundle rates, which, as discussed above, sets a fixed price for a group of products and services and allows the providers of the goods to negotiate how the payment will be shared. The bundling policy might encourage use of biosimilars [57].

Discussion and conclusion

In this paper, we have outlined why the US biosimilar market is likely to develop into a robust source of competition regardless of product naming, and further, why distinguishable naming, by itself, may have no discernible effect on the uptake of biosimilars. Rather, in examining biosimilar entry and market uptake in other regions, it is clear that other factors and financial incentives,

including manufacturers' rebates, beliefs, and behaviours of key stakeholders will drive both the entry of biosimilars into the market as well as the extent of its adoption.

In the small molecules market, a key driver of generic uptake in the US was the fact that brand-name manufacturers did not proactively respond to competition from generics [58]. Outside the US to date, we have seen considerable competitive response from branded biologicals, especially in the form of competitive pricing. While the generics market did not develop overnight, we see today the tremendous savings from generics, and expect relatively smaller but still important potential savings (on an absolute basis) from biosimilars. As observed in Europe, incentives sometimes deterred biosimilar uptake in the EU, despite the fact that shared names prevail in the region.

Ultimately, the financial incentives of stakeholders will determine how the market will develop and, following the case of generics; the US incentive system will likely evolve into a robust market for biosimilars. Both private and public payers are drawn to low prices, the government from an access and cost basis, and private payers from a profit basis. For example, bundling, especially for physician-administered drugs in Medicare Part B and private payers, will incentivize stakeholders to choose the least cost alternative for similar results.

Thus, in the face of compelling incentive schemes arising from both government reimbursement systems and third-party payers, it is unlikely that naming will have an impact on market uptake. Instead, potential cost savings to the US healthcare system from biosimilars will be achieved through careful structuring of reimbursement and payment systems.

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