Unlocking the Potential of Biosimilars

A Roadmap for Biosimilar Policy Sustainability

Biosimilar Policy Landscape & Sustainability Assessment

Belgium

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Introduction

The adoption of biosimilars can offer significant benefits to stakeholders yet has not been a uniform and equal process across countries. Biosimilar uptake has shown large discrepancies across (and sometimes within) countries.[i, ii] For example, in 2020 the uptake of infliximab biosimilars was 89% in the UK versus 6% in Japan.[iii] Biosimilar utilization can also vary significantly within countries. For example, in a 2021 US study, practice setting (outpatient hospital department vs office practice, and for-profit vs not-for-profit) was found to be a key driver in biosimilar use.[iv] A country's policy environment likely affects the variation in biosimilar success. Assessing the current biosimilar policy landscape and the extent to which current policies support long-term sustainability for biosimilars is critical to understanding the drivers of success, inefficiency and risk areas of biosimilars in any given country.

Methodology

This study presents a global analysis of the biosimilar-specific policies across a wide range of countries. Country-specific policy landscapes are summarised according to an assessment framework of nine policy areas depicted in **Table 1**. Country-specific desk research was conducted to draft policy landscapes and were subsequently validated through 1:1 interviews with country experts.

Table 1 - Policy area assessment framework

	**Manufacturing and R&D**	Policies incentivising local/regional manufacturing or investing in biosimilar R&D
	**Regulatory Approval**	Policies ensuring streamlined or accelerated regulatory pathways at national or regional level
	**Health Technology Assessment**	Policies allowing for reduced or differentiated HTA requirements for biosimilars
	**Pricing & Reimbursement**	Policies mandating price reductions for biosimilars or originator products or affecting reimbursement
	**Contracting**	Policies governing purchasing, including national/sub-national tendering and procurement of biosimilars
	**Biosimilar Education & Understanding**	Policies or initiatives supporting biosimilars education
	**Prescribing**	Policies affecting physician uptake and prescribing
	**Dispensing**	Policies at pharmacy level affecting dispensing of biosimilars
	**Monitoring**	Policies ensuring monitoring of safety and efficacy of biosimilars

Source: CRA

During 1:1 interviews, a sustainability assessment of each policy area was conducted to provide a 'biosimilar sustainability rating'. Based on a literature review, a scorecard was developed and tested with biosimilar policy experts. The scorecard summarises the potential multi-stakeholder benefits of biosimilars using a 5-point 'star rating' scale. (See **Table 2**). In addition to country-specific documents, a cross-country summary and global analysis of the long-term sustainability of biosimilar policies is published in the White Paper 'Unlocking the Potential of Biosimilars: A Global Roadmap for Biosimilar Policy Sustainability'.[v]

Table 2 – 5-point 'star rating' scale

★★★★★	The policy area is considered to be sustainable **for all stakeholders**
★★★★☆	Some **minor areas** for improvement were identified to result in a fully sustainable environment, however no unsustainable policies impact the area
★★★☆☆	Some **major areas** for improvement were identified to result in a fully sustainable environment, however no unsustainable policies impact the area
★★☆☆☆	There are sustainable policies in place which are being negated by the **presence of unsustainable policies** in the same/different policy area
★☆☆☆☆	The (lack of) policies in place are considered to **actively contribute to an unsustainable policy environment** for the majority of stakeholders

Source: CRA

Summary

	Manufacturing and R&D	Subject to EMA's guidelines	★★★★★	Biosimilars are held to the same manufacturing standards as originator products therefore quality is maintained. Manufacturing can begin before originator LoE facilitating supply at launch while still observing the full exclusivity period of the originator product.
	Regulatory Approval	Subject to EMA's guidelines	★★★★☆	Current evidence requirements are slightly streamlined and therefore can result in slightly faster access to biosimilars. However, recent research indicates that comparative clinical studies are not required for all biosimilar products and reducing the need for this evidence and/or implementing formally accelerated timelines could offer further regulatory efficiencies.
	Health Technology Assessment	Biosimilars do not need to undergo HTA, and their submission for reimbursement is slightly streamlined to 90 days. However, no added benefits / uptake drivers are obtained from this, and it is mostly perceived as a bureaucratic burden	★★★☆☆	Certain evaluation is required for biosimilars in order to grant reimbursement and inclusion in the system. Although there slight acceleration versus the process for innovative biologics, this still results in an additional burden for biosimilars to gain entry to some / all of the market
	Pricing & Reimbursement	Before a biosimilar is reimbursed, there is a 90-day registration period during which an official reimbursement decision is made. Biosimilars allowed to officially launch at originators' prices, but general cost-containment measures (e.g., '*biocliff*') apply steep discounts.	★★☆☆☆	Although accelerated vs the standard 120 day registration period, a 90-day delay to launch can be considered unnecessary and delaying the potential benefits of biosimilars. Cost-containment measures such as the '*biocliff*' decrease predictability for manufacturers and apply high discounts that decrease the benefits for sustainable prescribing incentive policies, which can also affect long-term competition and supply.
	Contracting	Single-winner tenders on the **inpatient level** with a high influence of price in its awarding criteria	Hospital ★★★☆☆ Outpatient	Awarding of tenders to single winners and high influence of price within their criteria could lead to unsustainable price erosion in the long-term, negating competition and potentially resulting in supply shortages

		Direct contracting of **outpatient biologics** between manufacturers and community pharmacies	★★☆☆☆	Direct contracting in theory can be a sustainable approach to biosimilar contracting in the long-term, however the lack of incentives in other parts of the Belgian system to prescribe biosimilar products decreases the long-term sustainability of the outpatient sector for biosimilar products. Combination of contracting with list pricing policy drives further price reduction. Moreover, input from different stakeholders is not accounted for such contracting decisions
	**Biosimilar Education & Understanding**	Education congresses organized by governmental health and pharmacy institutions however, national educational efforts are sporadic and not consistently applied	★★★☆☆	Despite national and international (EMA) efforts in the promotion of educational campaigns, the selection of the correct channels for information could further boost awareness around biosimilars and increase their access in the Belgian market. Further, consistent and targeted national campaigns over the long run could more effectively target misconceptions surrounding biosimilars to promote a more sustainable environment.
	**Prescribing**	No prescribing incentives for biosimilars in hospital No officially regulated biosimilar prescription quotas apply, although there are such quotas for 'low-cost medicines' in the outpatient setting. Pilot program for financial incentivisation promoted in 2019 in the outpatient setting.	Hospital ★★★★☆ ——— Outpatient ★★☆☆☆	In the hospital, tendering processes tend to favour originator biologics as hospitals are reimbursed fixed prices, but obtain larger confidential discounts on more expensive originator biologics ——— Although prescription quotas apply for low-cost medicines, general steep price discounts for biologics from pricing and contracting systems deprioritise biosimilars, undermining their value and reducing their access / uptake in the outpatient sector
	**Dispensing**	Automatic substitution prohibited, but higher mark-ups apply for more expensive biologics	★★☆☆☆	Higher mark-ups when dispensing biosimilars can increase their access and improve competition. However, official policies

				regulating substitution could improve pharmacists' flexibility without affecting biosimilars benefits. Given the inappropriate prescribing controls in Belgium, the sustainability of dispensing is limited.
	**Monitoring**	Following EMA's guidelines, biosimilars have the same pharmacovigilance requirements as their originators	★★★★☆	Although EMA sets equal guidelines for risk management assessment of biosimilars and originators, HCP involvement in pharmacovigilance upon switching can help improve biosimilars' perception and access

Key Successes, Areas for Improvement & Risk Areas

Key Biosimilar Policy Successes
▲ Claw-back regulations require annual compulsory payments for manufacturers at the end of the years. Current discussions are held to remove biosimilars from this policy ▲ There is political will to boost biosimilars' uptake
Key Biosimilar Policy Areas for Improvement
► A simplified pricing and reimbursement procedure would improve biosimilars' access to the market ► Health education for HCPs and patients have been developed but the information is not being transmitted/received. Better communication would raise awareness about safety and efficacy of biosimilars and overcome current loyalties to originator companies
Key Biosimilar Policy Risks
▼ Strong influence of price in tendering procedures results in continuous price decrease and erosion of the market ▼ While there is political will to boost biosimilars' uptake (but the combination of pharmaceutical companies and strong physician influence and independence for prescribing is interfering) ▼ Originator pharmaceutical companies are well established in the country and have strong supply chains across the whole European Union. This has been further enhanced by the COVID-19 pandemic, as the Cominarty vaccine is also produced in Belgium, therefore enhancing originators' marketing campaigns and their trust by the society.[vi]
Key Biosimilar Policy Priorities to Achieve Long-Term Sustainability in Belgium
1. Leveraging cross-country biosimilar policy environment learnings to engage with relevant stakeholders and promote biosimilar uptake in the country 2. TBDInvest in public health education and implement physician prescribing incentives

Policy Landscape Assessment

Manufacturing and R&D

No specific manufacturing or R&D policies identified in Belgium. Biosimilars are subjected to the same manufacturing principles that apply to their originators.

In the European Union, Good Manufacturing Practice (GMP) legislation is in place to govern biosimilar manufacture with some additional conditions versus small molecule manufacturing.

The manufacture of biological medicines tends to be more complex than for chemically-derived molecules. For biological medicines, some of the GMP requirements have been adapted to take into account their specific nature (e.g., use of appropriate aseptic techniques, refrigeration and other storage conditions, stability, transport etc.).[vii]

Any changes to the manufacturing process must be approved by the regulators and the extent to which subsequent comparability studies are requires will depend on the expected impact of quality, safety and efficacy of the medicine. Most often, analytical and functional data are sufficient, and clinical trials to prove safety and efficacy are not needed.

Regulatory Approval

Streamlined evidence requirements

Regulatory approval of biosimilars in Belgium follow the guidelines established by the European Medicines Agency (EMA) from 2006.[viii] The legal framework aims at demonstrating biosimilarity to the reference product by emphasizing physic-chemical analysis and loosening to a certain degree posterior clinical phases (e.g. phase II trials are generally not needed).[ix]

The centralised procedure for granting regulatory approval of biosimilars was first introduced by the EMA in 2004 (Regulation n. 726/2004).[x, xi] The Committee for Medicinal Products for Human Use (CHMP) regulates the authorization of biologics. The process aims at **providing enough evidence to demonstrate a high degree of similarity between the biosimilar and its reference product.** Therefore, no data needs to be acquired in terms of clinical benefit, as this is already provided by the reference product.[xii]

The process to demonstrate biosimilarity consists of three different steps. Firstly, thorough physic-chemical and biological analyses are developed to demonstrate proper quality of the product, as well as its toxicology. This is followed by a second step of non-clinical (pre-clinical) trials to compare pharmacodynamics and pharmacokinetics. The final step aims at demonstrating clinical comparability between the biosimilar and the reference product, and is developed via clinical trials to demonstrate safety, efficacy and immunogenicity.[xiii,xiv]

Immunogenicity data needs to be collected for one year before the CHMP allows marketing authorisation, and maintained later on for long-term pharmacovigilance purposes.[xv] Immunogenicity factors are listed in the guidelines (e.g., anti-drug antibodies (ADAs)) but risk assessments are encouraged to be developed on a product-specific basis, as immunogenicity is hard to foresee.[xvi] **Extrapolation of indications is permitted by the EMA once biosimilarity has been demonstrated for at least one, when the scientific justification is granted**.[xvii]

Health Technology Assessment

Simplified HTA submission requirements

In contrast to assessments carried out for innovative biologics, biosimilars are considered "class 2 products" and do not require any HTA. Their submission for reimbursement is slightly accelerated (90 days) but still requires certain simplified internal assessments. However, this is still perceived as an extra bureaucratic burden given the current pricing policies, and the fact that pharmaco-economic assessments are often disregarded in these reimbursement procedures, compared to the products' medical need and their therapeutic value.[xviii]

Pricing & Reimbursement

Accelerated reimbursement

Biosimilars can undergo an accelerated 90-days process for approval of reimbursement compared to the 180-days required for innovative biologics.

Originator Discounts at Biosimilar Launch

Innovative biologics generally undergo price reductions through cost-containment methods, also in place upon the entry of biosimilars. The National Institute for Health and Disability (NIHDI) has established '*cliffs*' for different categories as compulsory discounts that drugs must undergo once certain criteria are met – e.g., specific sales volumes for the '*volume cliff*' or certain years of reimbursement for the '*old medicines cliff*'. Such discounts are set at a maximum of 33.95%.[xix]

For biologics**, a price decrease of 20% is mandated for originators upon the entry of the first biosimilar to the market**. Moreover, even if biologics do not meet the other cliffs' criteria (*volume or old medicines*), biosimilars entry also triggers all price reductions explained above to be applied at once under the so-called '*biocliff*'.[xx] Such discounts have reached up to 38% for both originators and biosimilars.[xxi] These measures were intensified with the remodulation of the regulation of "biological medicines" (biologische geneesmiddelen) from the NIHDI in July 2020. As a result, both reference biologics as well as biosimilars are considered "low-cost medicines".[xxii]

The implementation of such measures has been criticised for the promotion of fast short-term savings without allowing for long-term efficacy and sustainability. Applying big discounts for both biosimilars and their originators does not allow for a proper different between both and negates fair grounds for competition. This decrease in competition is further emphasised by confidential managed entry agreements (MEAs) for originators, which also reduce the predictability for manufacturers applying for reimbursement of their biosimilar products.[xxiii]

Reference pricing

Prices for biosimilars in Belgium are negotiated individually with the NIHDI, being allowed to launch with their originators' official prices.[xxiv] However, they are equally submitted to the '*biocliff*' reductions. Further discounts arise from contracting procedures.

Partial coverage

Reimbursement is limited for patients who are prescribed originator biologics that have an existing biosimilar alternative. On the public pharmacy level, net prices for biologics are of public knowledge and calculated by subtracting possible co-payments to the list price. Therefore, the list price and the co-payments are also publicly available.[xxv]. In 2016, only 90% of the branded originator price was reimbursed by the NIHDI.[xxvi] This measure was further limited in 2019 to 85% reimbursement.[xxvii]

Contracting

Scope of contracts

While outpatient biologics are directly negotiated and contracted between manufacturers and insurance providers, biologics dispensed in hospitals are subjected to tendering processes. **These procedures are developed by hospital groups or individual hospitals**. In the outpatient sector, the net cost for insurance providers considers list prices minus patient co-payments.[xxviii]

Single-winner contracts

Tenders in Belgium are normally selecting **single winners**.[xxix]

Contract decision criteria

Tendering is regulated by the **law for public procurement,** which came into practice in July 2013 as an adaptation of the **European law 2004/18/EG**. **A minimum of 3 manufacturers need to participate** in the tendering procedure. The hospital can have some flexibility on the selection criteria, but they should always follow the **principles of equality, non-discrimination, transparency, and competition.**[xxx] Tenders in Belgium are highly awarded based on price. Originators in the country compete aggressively on this sense, willing to go for low prices, which acts as an extra burden for biosimilars contracting. As a result, the NIHDI came up with the 'Best value biologicals' program in 2019, which aimed at the proposition of follow-up measures to provide a level playing field for the fair competition between biosimilars and their originators. Some of the measures concerning contracting procedures proposed the softening of hospital tenders, as well as the implementation of gain sharing policies, where savings obtained in the healthcare system would be shared with those responsible for them. However, such propositions took second priority with the outbreak of the COVID-19 pandemic.[xxxi]

Biosimilar Education & Understanding

HCP and patient educational programs

In 2018, the Federal Agency for Pharmaceuticals and Health Products (FAAG) and the NIHDI organised an **education campaign to promote the prescription of biosimilars from healthcare practitioners and the knowledge from patients who receive the treatment**. The campaign was distributed via several media (e.g. radio, website, posters, banners and social media).[xxxii, xxxiii]

Educational efforts in Belgium are present, but they are organised sporadically and not in a continued consistent basis. As a result, the target audience does not seem to be reached and misconceptions about biosimilars exist, as patients tend to still consider them worse than lower-cost originators.

The 'Best value biologicals' program also came up with suggestions to drive better awareness around biosimilars and emphasised the need to provide continued and repeated educational campaigns across different channels.[xxxiv]

Additionally, the EMA's official webpage includes information about biosimilars and document to properly educate HCPs. Such documents were last updated in September 2019 and are currently available in 23 different languages. The information has been created gathering opinions from EU scientific experts (e.g., Doctors, nurses, pharmacists).[xxxv, xxxvi]

Patient educational programs

Additional to the online documents available in the EMA's webpage, other patient-friendly resources are available. An animated video was created, also in a wide scope of languages, clarifying key factors for these medicines for patients.[xxxvii] The European Commission has also created manuals to raise patient awareness around biosimilars.[xxxviii]

Prescribing

Prescription quotas

Official prescription quotas for biosimilars do not apply in the country. However, the agreement for the "Restart of Biosimilar Medicines in Belgium" (Doorstart voor biosimilaire geneesmiddelen in Belgie) establishes that a **minimum of 20% of treatments prescribed by physicians for naïve patients must include biosimilars**. This unofficial agreement was signed between the Minister of Social Affairs and Health, the pharmaceutical sector, and different medical institutions in January 2016.[xxxix] Biosimilar uptake is monitored by the NIHDI every three months.[xl]

Prescription quotas do apply for general low-cost medicines in the country from 2012.[xli] Low-cost drugs are defined based on cluster types and are those ones considered within the cluster price with up to further 5% of higher price, also including chemical drugs. **Financial penalties are applied when low-cost prescribing quotas are not met**.[xlii]

Financial incentives linked to biosimilar prescribing

There are currently no financial incentives to drive the prescription of biosimilars, although this has been tried in certain occasions. To increase the rate of prescription of etanercept and adalimumab, in 2019 the NIHDI established **financial incentives for those physicians reaching volume prescription targets of 5, 10 or 20% annually**. The associated compensation rates for hitting the three targets are 750, 1,000 and 1,500 euros, respectively.[xliii]

Dispensing

Automatic substitution

Automatic substitution of an innovative biologic by its biosimilar is prohibited in Belgium.[xliv] Moreover, its implementation is highly unlikely, given the lack of political will.

Regressive Retailer Mark-Ups

Dispensation fees exist for pharmacies, as well as manufacturers discounts.[xlv] Mark-ups are calculated as percentages of the pharmacy purchase price (PPP) and vary depending on manufacturing selling prices (MSP).[xlvi] **The more expensive the drug, the higher the mark-up**.[xlvii]

Monitoring

Pharmacovigilance measures

Following EMA's guidelines. No specific Belgian policies have been identified differentiating biosimilar monitoring from other pharmacovigilance efforts.

EMA's pharmacovigilance requirements for biosimilars are no different than those for biologics. The "list of medicines under additional monitoring" include both biosimilars, as well as those biologics approved after 2011 (and other groups of medicines). The products included in this list need to be labelled with an inverted black triangle in their documentation (e.g., Summary of Product Characteristics (SmPC) and label), and their manufacturer needs to provide a post-marketed pharmacovigilance system when applying for marketing authorisation, as well as the so-called "Risk Management Plan".[xlviii, xlix]

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