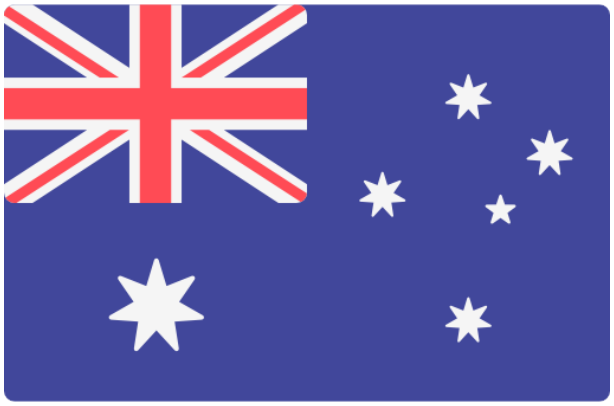
CRA Charles River Associates

Unlocking the Potential of Biosimilars

A Roadmap for Biosimilar Policy Sustainability

Biosimilar Policy Landscape & Sustainability Assessment

Australia



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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	No policies specific to biosimilar manufacturing have been identified. However, manufacture of biosimilars in Australia can begin in advance of the originator's loss of exclusivity. Otherwise, biosimilars are subject to the same quality and safety standards as other biologics	★★★★☆	Biosimilars are held to the same manufacturing standards as originator products therefore quality is maintained. However, manufacturing can only begin after originator LoE, which can result in slower access to the market and delay in the benefits realised by biosimilar entry
	**Regulatory Approval**	Streamlined clinical evidence requirements (including the option to reference data from comparisons versus products other than the originator) as well as the potential for indication extrapolation	★★★★☆	Although there are streamlined evidence requirements, potential for indication extrapolation and lower application fees, the regulatory assessment process is not accelerated
	**Health Technology Assessment**	Streamlined pharmacoeconomic requirements reduces barriers to assessment and reduce application fees	★★★★☆	HTA is required for biosimilars which ensures that uptake drivers are awarded consistently to biosimilar products (e.g. a-flagging status). The streamlining of evidence requirements simplifies the process, although the assessment process is not formally accelerated
	**Pricing & Reimbursement**	Mandated originator list discounts (25-60%) at biosimilar launch with reference pricing and additional progressive originator price discounts (every 5 years) both degrade biosimilar price benchmarks	★★☆☆☆	Reference pricing homogenises pricing across products based on the cheapest product not allowing for differentiation. Mandatory discounts erode price benchmarks, disincentivising ongoing innovation and future competition
	**Contracting**	Contracting varies across markets (hospital vs. community pharmacies); single-winner contracts used in some hospital pharmacies	★★★☆☆	Single-winner tenders restrict competition within the market, increase the risk of supply shortages and exclude smaller manufacturers. However, since procurement varies across stakeholder groups, this stimulates plurality meaning the negative impact of this is limited
	**Biosimilar Education & Understanding**	Biosimilar Awareness Initiative provides funding for HCP/patient education programmes	★★★☆☆	National educational efforts targeted at HCPs and pharmacists have likely contributed to broader uptake of biosimilar products, although significant misconceptions are still present in the market, especially among prescribers and patients
	**Prescribing**	Biosimilar switching and initiation are recommended and securing authorisation for	★★★★☆	Biosimilar switching is recommended, alongside patient involvement, but not

		biosimilar prescriptions are streamlined. INN must be used in prescriptions, but the brand can be specified, giving control of dispensing to physicians		mandated thus allowing physicians to have choice and flexibility in prescribing. Prescription of biosimilars over originators is encouraged by streamlined PBS authorisation however, there are no financial incentives to support uptake
	Dispensing	'A-flagging' enables automatic substitution of some biologics and there can be financial incentives for dispensing cheaper biologics	★★★☆☆	Physicians can specify the brand during prescribing, limiting substitution. No differential in patient co-pay for biosimilar versus the originator. However, poor physician education can lead to inappropriate restriction of substitution and diminished positive impacts of substitution policies
	Monitoring	No specific Australian policies have been identified differentiating biosimilar monitoring from other pharmacovigilance efforts. Regulatory approval can be contingent on biosimilars having risk management plans if they are requested, although they rarely differ from those of the originator. Surety of supply is driven by limits on dispensing >1 month of a prescription, increased stocking requirements for manufacturers and wholesalers	★★★★☆	Risk management plans support monitoring efforts, although batch-level traceability it limited, and supply guarantees can be opaque. The option to specify the brand in prescriptions diminishes the potential negative impact of INN prescribing. Measures have been implemented to ensure the surety of supply, mitigating against shortage risks

Key Successes, Areas for Improvement & Risk Areas

Key Biosimilar Policy Successes

- ▲ Various public health education initiatives with multiple different outputs
- ▲ Recommendations for biosimilar initiation and switching, alongside streamlined authorisation requirements
- ▲ The latest strategic agreements signed (expected to enter into force in 2022) between the GBMA, Medicines Australia and the Government has been updated to highlight the potential to implement additional uptake drivers for biosimilars in future

Key Biosimilar Policy Areas for Improvement

- ► Although HTA for biosimilars is accelerated (and cheaper) given that economic evaluation is not required; biosimilars still must undergo a formal HTA process to launch in Australia after TGA approval. Allocation of uptake drivers (e.g. 'A-flagging') is also contingent on the HTA process. There could be potential to streamline regulatory and HTA processes and provide access to biosimilars more efficiently
- ► Lack of differentiation in co-payments for biosimilars and originator biologics; introduction of lower co-payments for biosimilars would provide a financial incentive for patient use
- ► Therapeutic reference pricing where the benchmark is set by the lowest cost brand
- ► Financial incentives for dispensing pharmacists could be aligned with physician incentives and formalised to encourage increased biosimilar uptake

Key Biosimilar Policy Risks

- ▼ There is a lack of biosimilar awareness and education amongst policymakers and patients; in some cases, biosimilars are perceived and treated in a similar manner to generics, leading to potentially unsustainable practices
- ▼ Statutory price reduction mechanisms which do not differentiate between biosimilars and generics, introducing aggressive launch discounts for the first biosimilar, unsustainably eroding pricing
- ▼ New stockholding requirements dictate that from 2023, manufacturers will be required to hold 4-6 months of stock, which is significantly more challenging for biosimilars (relative to generics) given their higher prices

Key Biosimilar Policy Priorities to Achieve Long-Term Sustainability in Australia

1. Align incentives across all key stakeholders, including physicians, pharmacists and patients
2. Decrease the co-payment for patients who choose a biosimilar, so as to incentivise patients directly
3. Increase multi-disciplinary decision-making regarding dispensation of biosimilars

4. Optimise existing pricing and reimbursement policy to mitigate impact of erosion driven by mandatory discounts

Policy Landscape Assessment

Manufacturing and R&D

Manufacturing Exemption Waiver

The manufacturing of biosimilars (and generics) can begin prior to the expiry of the originator's patent exclusivity in a similar manner to that permitted by EU legislation.

Regulatory Approval

Streamlined evidence requirements

In Australia, the Therapeutic Goods Administration (TGA) provides regulatory approval for biosimilars. This is provided on the basis that there are not clinically or therapeutically meaningful differences between the biosimilar and the originator (reference medicine).[vi] Generally, the TGA will streamline clinical evidence requirements by accepting a Phase III clinical trial for a single indication as be sufficient to confirm biosimilarity. Furthermore, once biosimilarity has been established, it may be possible for a biosimilar to be approved for other indications by so-called 'indication extrapolation' from the reference product's data.[vii, viii]

In order to minimise duplication of trials, it may also be possible to conduct certain clinical studies and *in vivo* non-clinical studies comparing the biosimilar to a medicine that is not registered in Australia.[ix]

Health Technology Assessment

Simplified HTA submission requirements

Where a biosimilar's indicated population is not extended beyond that of the originator, biosimilars are eligible to make a 'Category 3' submission to the Pharmaceutical Benefit Advisory Committee (PBAC) prior to their assessment. This submission route still results in an assessment of clinical need and effectiveness but excludes economic evaluation. Furthermore, this submission route also requires a lower application fee.[x]

Pricing & Reimbursement

Reference pricing

PBAC applies a cost-minimisation approach to approved biosimilars, preventing them from attaining a list price premium.[xi] As per the Australian National Health Act 1953 Subsection 85C, different brands of the same medicine must have the same list price.[xii] Importantly, the lowest priced brand (e.g., a biosimilar) listed on the PBS sets the benchmark list price which applies to all brands (e.g., the originator).

Originator Discounts at Biosimilar Launch

The new industry agreements have increased the mandated originator discounts, increasing the maximum potential list discount from 25-40% to 25-60%. This discount applies to the originator once the first biosimilar launches, and through Special Pricing Agreements defines maximum pricing of biosimilars.[xiii]

Progressive price discounts

Originators undergo statutory price reductions five (5%), ten (5%) and fifteen (26.1-30%) years after launch.[xiv] Originators are only subject to the reduction after fifteen years if a biosimilar competitor has not yet launched. Thus, if a biosimilar launches after fifteen years, the originator will experience a 26.1-30% discount, followed by a 25-60% discount, significantly lowering the price benchmark.

An additional pricing mechanism, called 'price disclosure', exists to ensure that increased competition within the market is translated into list price discounts applied across the various competing brands. Every 6 months, the government requires manufacturers to provide the Department of Health with their current list price used with wholesalers and pharmacies. If this list price is more than 10% below the price listed on the PBS, then the PBS listed price will be reduced. Thereby preventing the government from subsidising medicines for more than they are being sold to wholesalers and pharmacies.[xv]

Contracting

Contract scope

Contracting occurs in two markets in Australia, the hospital market – which is heterogenous and operated at the state level – and the community pharmacy level.

Single-winner contracts

Procurement strategies differ from state to state in public hospitals, hence there are different contracting approaches used.[xvi] In some hospital pharmacies, competitive single-winner tenders are used to drive competition and hence reduce procurement costs. These tender processes have been observed for epoetin biosimilars used to treat renal anaemias.[xvii]

Differences between the suppliers selected at hospital tenders and community pharmacies contracts can cause discrepancies for patients when they try to access the same brands in both settings, which is not always granted. Therefore, more consistent predictable methods have been claimed as necessary.

Biosimilar Education & Understanding

HCP and patient educational programs

In May 2015, the Biosimilar Awareness Initiative was launched by the Department of Health (as a part of the Pharmaceutical Benefits Scheme Access and Sustainability Package) to support awareness of, and confidence in, the use of biosimilar medicines for health care professionals and consumers.[xviii] This involved signing a strategic agreement with the Generic and Biosimilar Medicines Association (GMBA).

A further budget commitment was made by the government in 2018 to support the Generic and Biosimilar Medicines Association (GMBA) with a $5 million grant, to complement and extend the Department's Biosimilar Awareness Initiative.

Overall, through this initiative, a variety of educational resources (e.g. the Biosimilar Hub website) have been created, which span across a range of media (e.g., infographics and videos).[xix] Furthermore, molecule-specific fact-sheets are even created, which provide both HCPs and patients with tailored information.

Nevertheless, awareness and understanding of biosimilar value could still be improved, especially among patients, as these are reported to be the group with the biggest misconceptions.

Prescribing

Clinical guidelines and prescriber-initiated switching

As part of the 2017 Budget process the Government reached agreement with Medicines Australia, the Generic and Biosimilar Medicines Association and the Pharmacy Guild of Australia to implement biosimilar uptake drivers. One of these drivers relates to encouraging the prescription of biosimilars rather than the reference, originator brand, particularly in the case of treating naïve patients. The choice to initiate or switch is not mandatory and is a decision that is made by the physician in discussion with the patient.[xx]

This recommendation complements the active ingredient (international non-proprietary name) prescribing that physicians must adhere to. Despite this, it is still possible for physicians to specify that the branded originator must be used, preventing substitution. Mechanisms to actually track this have been proposed by the expert as a mean to control physicians' preferences for originator brands, which currently still remains as a barrier for biosimilars adoption.

Generally, biologics listed on the PBS require prior authorization or approval (from the PBS) to be prescribed. In the 2017 Budget, a simpler and faster approval process for prescribing biosimilar brands was outlined. Consequently, biosimilars do not require the same written authorization that originator biologics are subjected to, hence the process required for biosimilar prescription is streamlined and less restricted than originators.[xxi]

Dispensing

Automatic substitution

Australia's PBAC determines interchangeability for biosimilars on a case-by-case basis and those that are deemed interchangeable are given 'a-flag' designation. Automatic substitution at the pharmacy level was introduced in 2015 after the signing of the 6th Community Pharmacy Agreement (6CPA) by the Pharmacy Guild and The Australian Government. Consequently, pharmacists can substitute biosimilars that have been given this designation without informing the prescribing physician.[xxii] Generally, all biosimilars for a given originator are 'a-flagged', as has been seen for etanercept (Brenzys), infliximab (Inflectra, Renflexis) and adalimumab (Amgevita, Hadlima).[xxiii] Despite this designation, if the physician ticks the box 'brand substitution not permitted', substitution at the pharmacy-level is not permitted.

Regressive retailer mark-ups

When dispensing medicines cheaper than the reimbursement price, pharmacists in Australia are allowed to keep the difference between the wholesale price and reimbursement price. Given that some biosimilars are now 'a-flagged' (automatic substitution allowed), this may provide an indirect incentive to dispense cheaper biosimilars.[xxiv]

Monitoring

Pharmacovigilance measures

Typically, in order to gain regulatory approval, the TGA require biosimilar manufacturers to submit risk management plans, which are then evaluated on a case-by-case basis. Although these plans are broadly consistent with those outlined for the reference originator product, they can vary.[xxv]

Supply monitoring

During the pandemic, in order to ensure that supply shortage risks were mitigated, a restriction was placed on dispensing. Pharmacists agreed (with the Government) to not dispense patients more than one month of their prescription in advance. This measure did not arise from a policy update, but a less formal agreement.

Additional measures include new stockholding requirements which dictate that from 2023, manufacturers will be required to hold 4-6 months of stock of biosimilars or generics. Furthermore, pharmaceutical wholesalers are required to stock all available brands of a molecule, ensuring both patient access to these treatments and variety in supply.

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