Building on the experience and success of biosimilar medicines

Biosimilar medicines are increasingly becoming an integral part of modern healthcare systems, so what does the future hold?
Biosimilar medicines are internationally recognized for expanding access to life-changing treatments

“Globally, regulators have confidence in the rigour of the scientific review and approval process for biosimilars.”¹

International Coalition of Medicines Regulatory Authorities (ICMRA) Statement about confidence in biosimilar products

“The Committee recognized that increased availability of biosimilars could lead to greater market competition, improved access and reduced costs for patients and health systems”.⁴

23rd WHO Expert Committee on the Selection and Use of Essential Medicines 2021

Reference:
Health Ministers recognize the value and benefits of biosimilar medicines use for healthcare.

7 of the top 10 most expensive medicines on the PBS are all from the bio family. That's why what's occurring with biosimilars is so important, because it helps to expand the sustainability of the health system & helps to bring down the cost of these medicines.

October 2, 2019, NSW Parliament House

Biosimilars are a necessary step to ensure PharmaCare provides existing coverage for more people and funds new drugs well into the future.

The Honourable Greg Hunt
Former Health Minister
Australia

The Honourable Adrian Dix
Minister of Health
Province of British Columbia (B.C.), Canada
Globally, there is a huge opportunity for biosimilar medicines to provide competition to existing biological medicines.

### Percentage of global biological medicine sales by region

<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>58%</td>
</tr>
<tr>
<td>Europe</td>
<td>23%</td>
</tr>
<tr>
<td>Japan</td>
<td>5%</td>
</tr>
<tr>
<td>Other</td>
<td>14%</td>
</tr>
</tbody>
</table>

### Percentage of global biosimilar medicine sales by region

<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>38%</td>
</tr>
<tr>
<td>Europe</td>
<td>52%</td>
</tr>
<tr>
<td>Japan</td>
<td>4%</td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
</tr>
</tbody>
</table>

Experience of biosimilar medicines in Europe and the USA is expected to support faster uptake in other regions.
Opportunity to generate competition in the biologics space with 600 biosimilar approvals covering over 10 therapeutic areas

A. Canada  
B. USA  
C. Brazil  
D. Argentina  
E. European Union  
F. Switzerland  
G. Serbia  
H. Montenegro  
I. Jordan  
J. South Africa  
K. Japan  
L. South Korea  
M. Malaysia  
N. Taiwan  
O. Australia  
P. Singapore

Number of biosimilar approvals

Source of data: IGBA membership, Swissmedic and HSA Singapore
Switching biological medicines is considered safe\(^1\)

- **Europe is leading the way** in switching from the reference to a corresponding biosimilar medicine\(^2\)
- European Public Assessment Reports (EPARs), available on the EMA website, provide **substantial evidence** for the safety of a switch\(^2\)
- In Japan, a switching study from reference product filgrastim to the biosimilar demonstrated the same clinical efficacy and safety, but at a **reduced cost**\(^3\)
- **Large clinical experience** in Europe supports switching not only between new versions of the same product, but also between a reference and its biosimilar medicine\(^2\)
- The lack of safety signals in Europe provides further **reassurance** of the safety of switching between the reference and the biosimilar medicine\(^2\)
- The available switching data (over 170 studies) do not indicate that switching from a Reference Product to a Biosimilar is associated with any major efficacy, safety or immunogenicity issues\(^4\)
- A prescribing healthcare professional **transferring** a patient on treatment from an originator to a biosimilar medicine is an **accepted clinical practice in many countries**\(^5\)

Under the supervision of the treating physician, patients can be safely switched from the reference product to the biosimilar medicine and vice versa\(^3\)

Widespread support for switching biosimilar medicines under supervision of a healthcare person

National guidance

Regulatory guidance

Clinical guidance*

Authorities supporting physician-led switching
No public position available

Source: Medicines for Europe Internal Biosimilar Mapping
* Medicines for Europe Overview of biosimilar physician-led switching (EU) updated Sept 2020
Switching studies confirm no differences in safety, efficacy or immunogenicity (2018)

Scientific literature (1993-2017) on switching

<table>
<thead>
<tr>
<th>Single or multiple switch</th>
<th>Reference → Biosimilar</th>
<th>90 studies</th>
<th>7 molecules</th>
<th>14 indications</th>
<th>14,225 individuals</th>
</tr>
</thead>
</table>

**Unchanged risk** of **immunogenicity**-related safety concerns or **diminished efficacy** after switching

- Huge majority of **single switch** studies **did not report differences in safety, efficacy or immunogenicity** compared to patients not switched.
- Small number (three) of **multiple switch** studies published, but likewise **no differences detected**.

No major efficacy, safety, or immunogenicity issues when switching from a reference product to a biosimilar (2020)

A Systematic Review on Switching (178 studies)
Reference to Biosimilar Product

Randomized controlled trials | Real-world evidence

“No major efficacy, safety, or immunogenicity issues when switching from a reference product to a biosimilar (2020)"

Switching between versions of a given biologic medicine is safe and effective

- The choice to switch a patient's therapy from one biosimilar to another is becoming increasingly feasible as a growing number of biosimilars of the same reference biologic are introduced onto the market.

- Switching from a reference biologic to a biosimilar may be explored in a randomized clinical setting, but switching from one biosimilar to another is more likely to be assessed in real-world settings including observational studies and registries.

- This systematic review outlines studies conducted to date on switching between two biosimilars of the same reference biologic, suggesting that these switches are a safe and effective clinical practice that is not associated with loss of effectiveness or an increase in adverse effects.

“Available data suggests that biosimilar-to-biosimilar switching is a safe and effective clinical practice, [...]. No reduction in effectiveness or increase in adverse events was detected in biosimilar-to-biosimilar switching studies conducted to date.”

References: 1. Switching from One Biosimilar to Another Biosimilar of the Same Reference Biologic: A Systematic Review of Studies (springer.com); Accessed July 2022
Vast pharmacovigilance data unambiguously supports sameness in efficacy & safety profiles

“The overall identifiability of biologicals between 2011-2019 was found to be 91.5%”

- Introducing biosimilar medicines to the market does not seem to affect identifiability of biological products in EudraVigilance Pharmacovigilance reports
- Having a larger number of biosimilars within the same INN does not correlate with poorer identifiability
- Identifiability is generally better when Adverse Drug Reactions are reported by patients then when they are reported by healthcare professionals

“As of January 2021, [...] Pharmacovigilance activities, which monitor the safety of all medicines, have not detected any serious safety concerns related to the use of biosimilars in the EU. Moreover, no safety or efficacy differences have been identified between reference products and their corresponding biosimilars.”

Overview of biosimilar physician-led switching (EU), updated in Oct. 2021

A number of medical societies have revised their initial positions and recommendations on the use of biosimilar medicines, recognising the positive clinical experience and benefits for patients.
“Switching a stable patient from a reference product to a biosimilar product is appropriate if the patient and physician agree to it.”
Transitioning approach to biosimilar medicines in six Canadian Provinces and one Territory

- British Columbia¹, Alberta², Saskatchewan³, Quebec⁴, New Brunswick⁵, Nova Scotia⁶ and the Northwest Territories⁷ have implemented well-controlled biosimilar switching policies, saving hundreds millions of dollars that have been reinvested into their healthcare systems.

- Switches have been made for such products as adalimumab, enoxaparin, etanercept, infliximab, insulin aspart, insulin glargine, insulin lispro and rituximab.

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The total clinical experience with biosimilar medicines exceeded 2 billion patient treatment days in Europe.

Over the last 10 years, the cumulative patient treatment days for EU approved biosimilar medicines have doubled every ~1.5 years\(^1\)

In the US, biosimilar medicines have been used in 121 million days of patient therapy, and have resulted in almost 10 million additional days of patient therapy.\(^2\)

Increasing experience with biosimilar medicines supports faster uptake of subsequent new biosimilar medicines

- Infliximab was the first biosimilar monoclonal antibody (mAb) to be launched in Europe
- Uptake of a subsequent complex biosimilar, etanercept, was generally similar or improved compared with that of infliximab

Comparison of post-launch market share of biosimilar infliximab with that of etanercept for the same time period

<table>
<thead>
<tr>
<th>Country</th>
<th>Infliximab</th>
<th>Etanercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands Month 1</td>
<td>0.1%</td>
<td>5.2%</td>
</tr>
<tr>
<td>Denmark* Month 3</td>
<td>5.8%</td>
<td>49.3%</td>
</tr>
<tr>
<td>Sweden Month 4</td>
<td>18.0%</td>
<td>85.3%</td>
</tr>
<tr>
<td>Norway Month 5</td>
<td>14.2%</td>
<td>57.6%</td>
</tr>
<tr>
<td>Germany Month 5</td>
<td>10.0%</td>
<td>8.9%</td>
</tr>
<tr>
<td>UK Month 5</td>
<td>7.7%</td>
<td>6.6%</td>
</tr>
</tbody>
</table>

*Denmark data from MIDAS monthly restricted database

In Europe, biosimilars have captured 7% more of the biologics market\textsuperscript{1} over a 5-year period.

In the last 5 year period, biosimilar market growth in the EU mainly relates to immunology and oncology biosimilar market growth.

Source: 1. IQVIA MIDAS MAT Q2 2020; Country cohort includes 30 countries within Europe Economic Area - Biologics market by value
The growing number of available biologic therapies offers future opportunities for biosimilar medicines development.

Over the next 10 to 15 years, more than 30 biologic medicines (mainly monoclonal antibodies) will lose market protection and open to biosimilar competition in existing and new therapy areas, including for orphan indications.

Sources: Biosimilar medicines group (Medicines for Europe) non-exhaustive compilation based on publicly available information (Oct 2020)
Availability of biosimilar medicines improves the security of the supply chain

- The FDA and EMA have identified manufacturing problems, delays in supply, and lack of available active ingredients as the most frequent causes of drug shortages\(^1\).

- Drug shortages can compromise patient safety and clinical outcomes, and increased healthcare costs, due to delays or changes in treatment regimens\(^1\).

- Biosimilar medicines help prevent future biologic shortages and ensure access to effective and safe treatment options\(^1\).

“[...] the biosimilar market will see a more diverse range of companies, greater competition, and improved supply chain security.”\(^2\)

Alex Kudrin, Biopharmaceutical Consultant, United Kingdom

Biosimilar medicines offer improved access to more cost-effective healthcare, today and in the future

Abbreviation: EMA, European Medicines Agency; FDA, Food and Drug Administration.

Summary: Building on the experience and success of biosimilar medicines

The benefits offered by biosimilar medicines are internationally recognized\(^1\)

Around the world, multiple biosimilar medicines have been approved\(^2\text{-}^6\)

Switching from a reference product to a biosimilar medicine is considered safe\(^7\)

Experience with biosimilar medicines improves uptake\(^8\)

A strong pipeline supports the continuous introduction of new biosimilar medicines\(^1\)

Availability of biosimilar medicines safeguards the supply chain, ensuring patient access to key therapeutics