Chapter 6

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)**

"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**

"Biosimilars can provide more treatment options for patients, and possibly lower treatment costs, enabling greater access for more patients"[2]

Dr Janet Woodcock, Director, Centre for Drug Evaluation and Research, Food and Drug Administration (FDA)

"The potential savings from an uptake of biosimilar medicines are very relevant for tackling inequalities in #cancercare"[3]

Stella Kyriakides
Commissioner for Health and Food Safety
European Commission

Biosimilar medicines are cost-effective therapeutic alternatives to reference biological products[1]

Reference: 1. ICMRA statement about confidence in biosimilar products (for healthcare professionals) Available at https://bit.ly/2IXwwTJ. Accessed October 2020;
2. Woodcock J. Biosimilars Implementation. Accessed March 2020; **3**. BIOS21 keynote speech, Medicines for Europe, May 2021.; **4**.WHO Executive summary of the Selection of Essential Medicines 2021. Accessed July 2022

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

The Honourable Greg Hunt
Former Health Minister
Australia

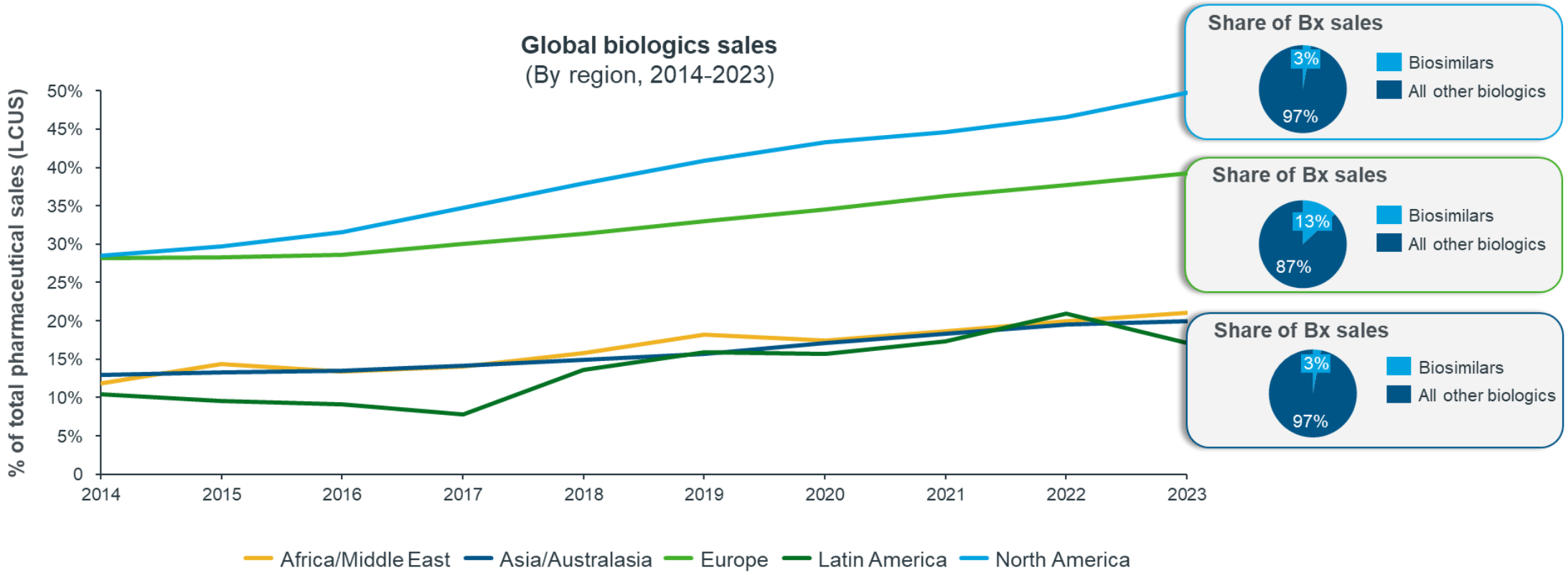
7 of the top 10 most expensive medicines on the PBS are all from the bio family. That's why what's occurring with biosimilars is so important, because it helps to expand the sustainability of the health system & helps to bring down the cost of these medicines

October 2, 2019, NSW Parliament House

The Honourable Adrian Dix
Minister of Health
Province of British Columbia (B.C.), Canada

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

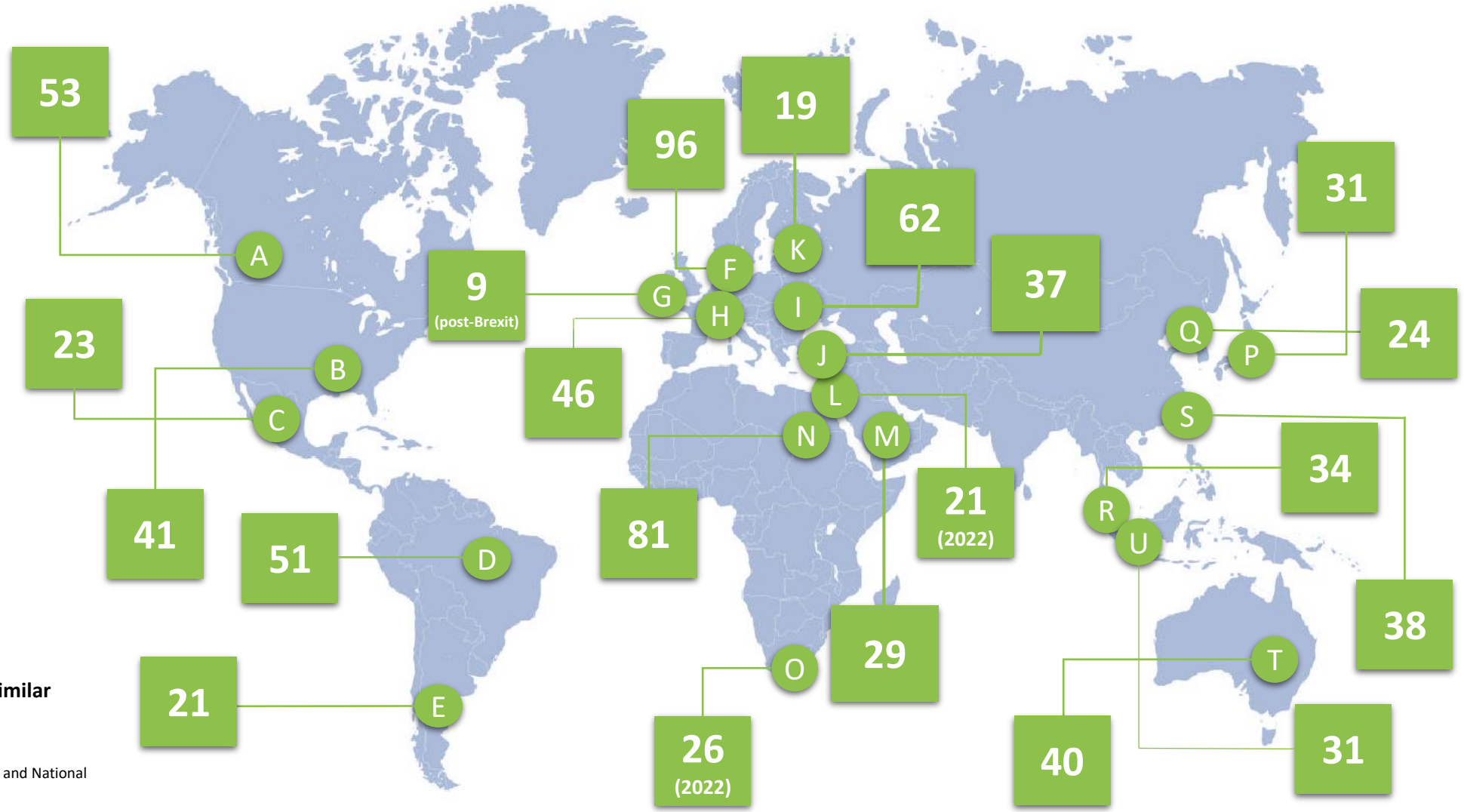
Globally, there is a huge opportunity for biosimilar medicines to provide competition to existing biological medicines



Europe and North America dominate on biological medicines use. Experience with biosimilar medicines in these regions is expected to support faster uptake in other regions

Reference: IQVIA, MIDAS MAT Q2 2023;, Retail and Hospital; Biocomp, biosimilars; Rx only.

Opportunity to generate competition in the biologics space with more than 800 biosimilar medicines covering over 10 therapeutic areas



A. Canada
B. USA
C. Mexico
D. Brazil
E. Argentina
F. European Union
G. UK
H. Switzerland
I. Serbia
J. Turkey
K. Montenegro
L. Jordan
M. Saudi Arabia
N. Egypt
O. South Africa
P. Japan
Q. South Korea
R. Malaysia
S. Chinese Taipei
T. Australia
U. Singapore

Number of biosimilar approvals

Source of data: IGBA membership and National Regulatory Authorities

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Switching biological medicines is considered safe[1]

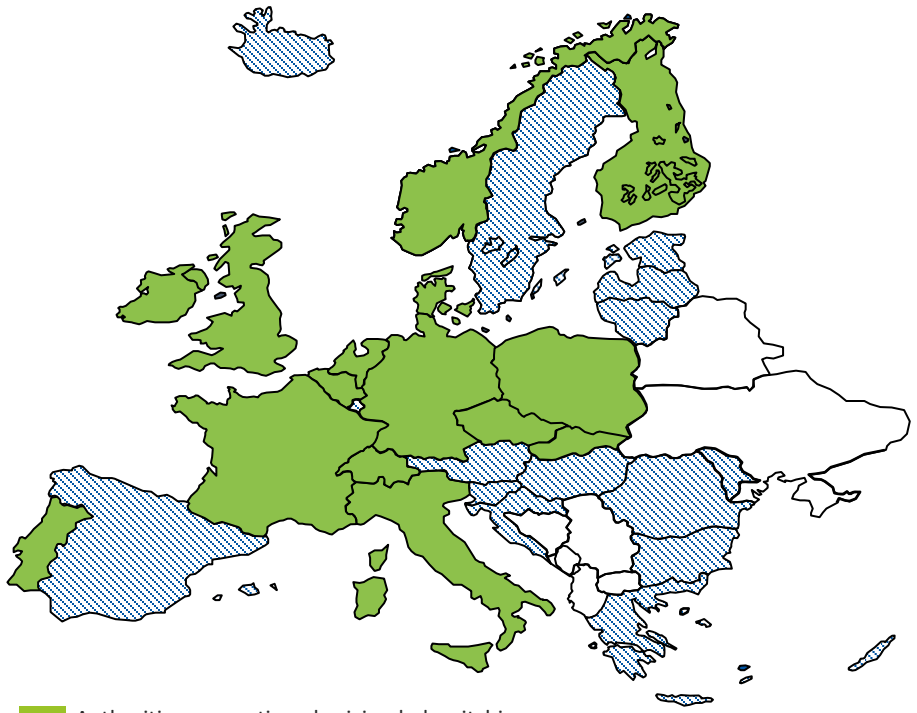
- **Europe is leading the way** in switching from the reference to a corresponding biosimilar medicine[2]
- European Public Assessment Reports (EPARs) , available on the EMA website, provide **substantial evidence** for the safety of a switch[2]
- In Japan, a switching study from reference product filgrastim 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 has become **clinical practice in many countries**[5,6]

Under the supervision of the treating physician, patients can be safely switched from the reference product to the biosimilar medicine and vice versa[3]

References: ; **1.** Glintborg B, et al. *Ann Rheum Dis* 2017; [Epub ahead of print]; **2.** Kurki P, *et al. BioDrugs.* 2017;3(2):83–91;
3. Kamada I, et al. *RSMP* 2017;7(1):3–15. **4.** Source: Barbier, Ebbers, Declerck, Simoens, Vulto and Huys - The Efficacy, Safety , and Immunogenicity od Switching Between Reference Biotherapeutics and Biosimilars: A Systematic Review (2020). Clinical Pharmacology & Therapeutics. https://doi.org/10.1002/cpt.1836 . Accessed November 2020; **5.** ICMRA statement about confidence in biosimilar products (for healthcare professionals). Available at https://bit.ly/2IXwwTJ, Accessed October 2020.; **6.** UK MHRA Guidance on the licensing of biosimilars (Nov 2022) https://www.gov.uk/government/publications/guidance-on-the-licensing-of-biosimilar-products/guidance-on-the-licensing-of-biosimilar-products, Accessed Sept 2023.

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

National guidance



Authorities supporting physician-led switching

No public position available

Regulatory guidance

BioDrugs
DOI 10.1007/s40259-017-0210-0

CURRENT OPINION

Interchangeability of Biosimilars: A European Perspective

Pekka Kurki[1] · Leon van Aerts[2] · Elena Wolff-Holz[3] · Thij
Venke Skibeli[5] · Martina Weise[6]

"In our opinion, switching patients from the original to a biosimilar medicine or vice versa can be considered safe."

Clinical guidance*

ESMO Open
Cancer Horizons

Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers

Josep Tabernero,[1] Malvika Vyas,[2] R
Paolo G Casali,[6] Andres Cervantes,
Jacek Jassem,[10] George Pentherou
Christoph C Zielinski,[14] Rolf A Stahe
Keith McGregor,[2] Fortunato Ciardiel

ECCO Position Statement

ECCO Position Statement on the Use of Biosimilars for Inflammatory Bowel Disease—An Update

Silvio Danese,[a,b] Gionata Fiorino,[c] Tim Raine,[d] Marc Ferrante,[e]
lian Panes,[k]

JCC

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases

Jonathan Kay,[1] Monika M Schoels,[2] Thomas Dörner,[3] Paul Emery,[4] Tore K Kvien,[5] Josef S Smolen,[2,6] Ferdinand C Breedveld,[7] on behalf of the Task Force on the Use of Biosimilars to Treat Rheumatological Diseases

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)

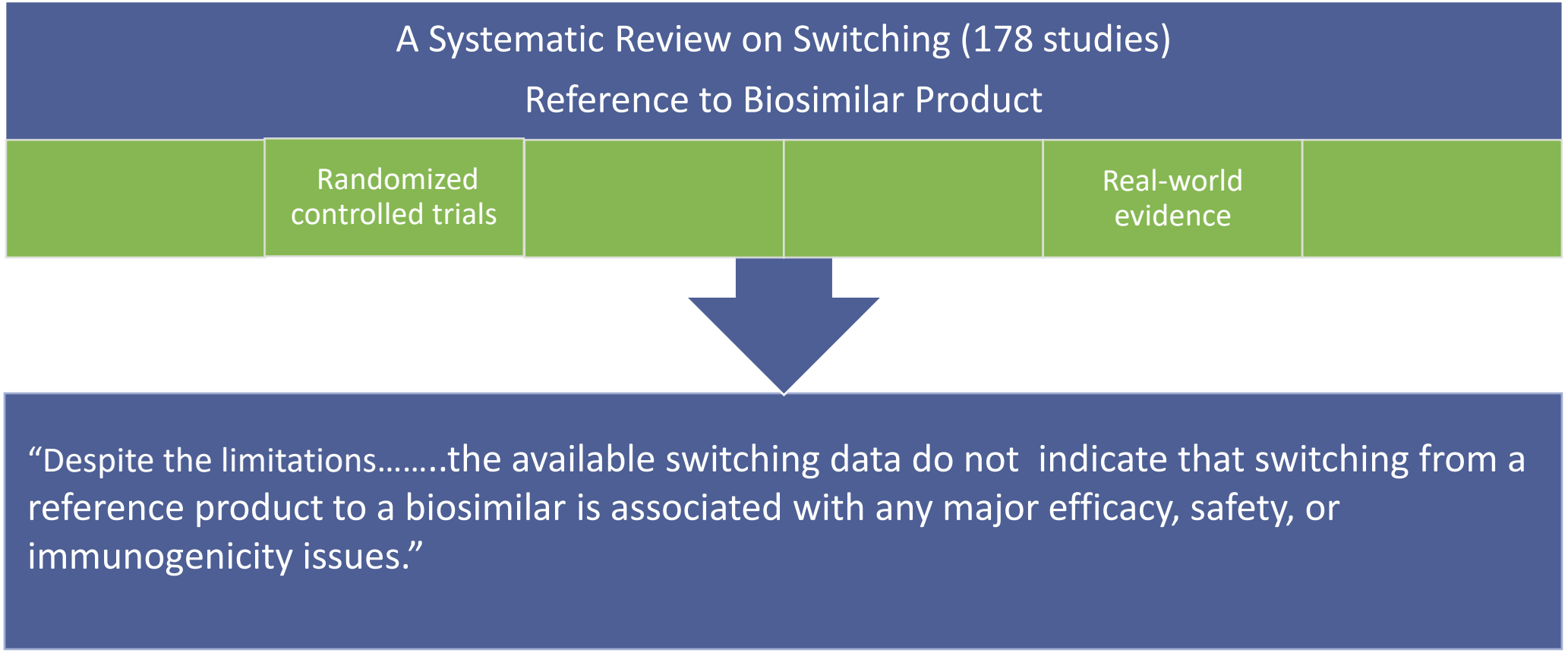
Scientific literature (1993-2017) on switching					
Single or multiple switch	Reference → Biosimilar	90 studies	7 molecules	14 indications	14 225 individuals

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**.

Source: H. P. Cohen – Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes

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



Source: L. Barbier, H. Ebbers, P. Declerck, S. Simoens, A. Vulto, I. Huys –The Efficacy, Safety, and Immunogenicity of Switching Between Reference Biopharmaceuticals and Biosimilars: A Systematic Review Clin Pharmacol Ther. 2020 Oct; 10.1002/cpt.1836

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

"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."*

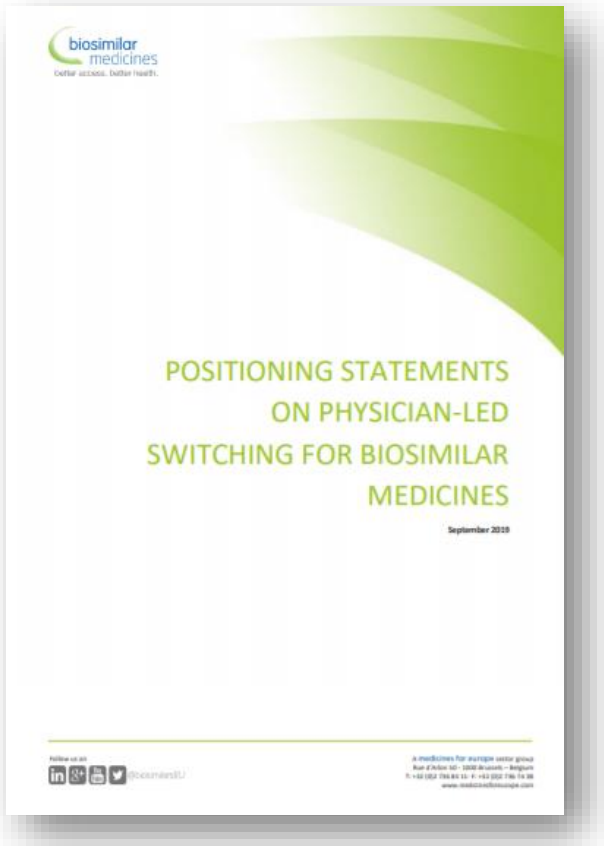
The **overall identifiability of biologicals** between 2011-2019 was found to be

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

Source: Wolff-Holz, E. et al - Identifiability of biologicals: an analysis using the EMA adverse drug reaction database, EudraVigilance (2021) Accessed Sept 2021

EU: Clinical use and experience inform medical societies' positions



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

2015

eular

BIOSIMILARS: WHAT DO PATIENTS NEED TO CONSIDER?

2017

Ann Rheum Dis. 2018 Feb;77(2):165-174. doi: 10.1136/annrheumdis-2017-211937. Epub 2017 Sep 2.

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases.

Kay J[1], Schoels MM[2], Dörner T[3], Emery P[4], Kvien TK[5], Smolen JS[2,6], Breedveld FC[7]; Task Force on the Use of Biosimilars to Treat Rheumatological Diseases.

⊕ **Collaborators (18)**

⊕ **Author information**

Abstract

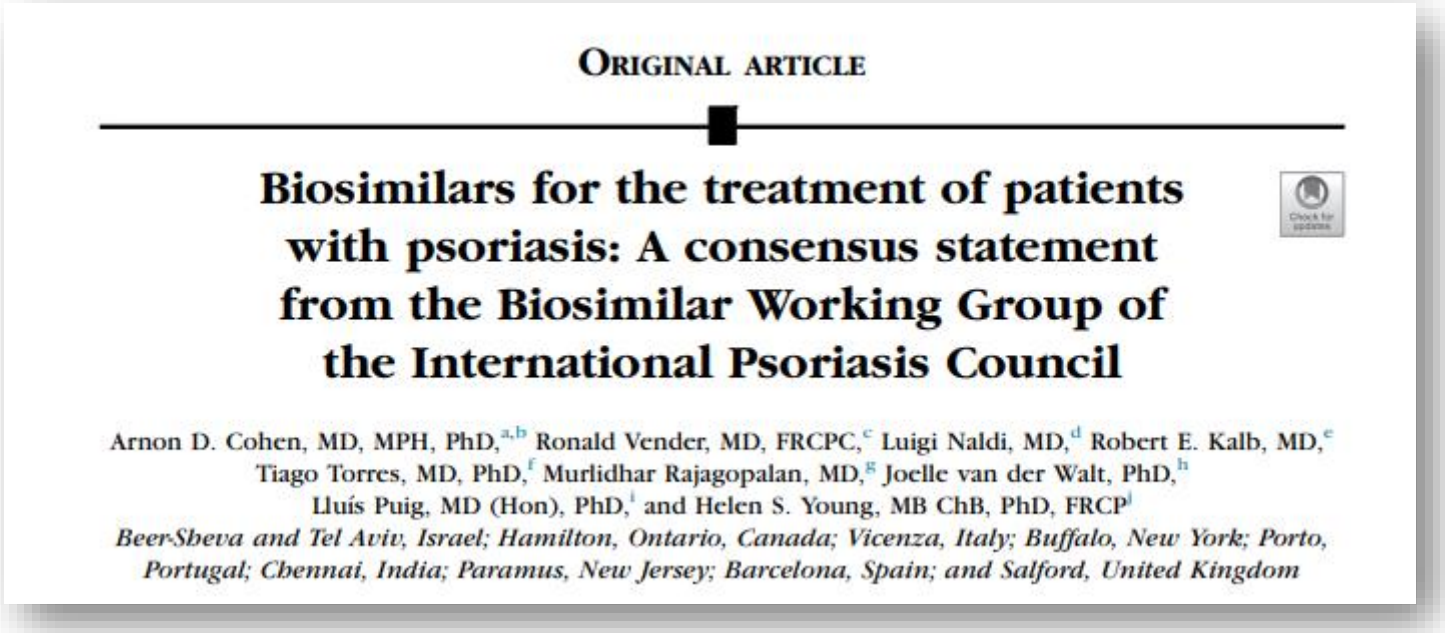
The study aimed to develop evidence-based recommendations regarding the evaluation and use of biosimilars to treat rheumatological diseases. The task force comprised an expert group of specialists in rheumatology, dermatology and gastroenterology, and pharmacologists, patients and a regulator from ten countries. Four key topics regarding biosimilars were identified through a process of discussion and

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

EULAR (European League Against Rheumatism) EULAR 2018 position: https://www.eular.org/myUploadData/files/biosimilars_paper_updated_2018_09_14_dw.pdf

International Psoriasis Council guideline endorses switching as clinical practice

- *"Switching a stable patient from a reference product to a biosimilar product is appropriate if the patient and physician agree to it."*



ORIGINAL ARTICLE

Biosimilars for the treatment of patients with psoriasis: A consensus statement from the Biosimilar Working Group of the International Psoriasis Council

Arnon D. Cohen, MD, MPH, PhD,[a,b] Ronald Vender, MD, FRCPC,[c] Luigi Naldi, MD,[d] Robert E. Kalb, MD,[e] Tiago Torres, MD, PhD,[f] Murlidhar Rajagopalan, MD,[g] Joelle van der Walt, PhD,[h] Lluís Puig, MD (Hon), PhD,[i] and Helen S. Young, MB ChB, PhD, FRCP[j]

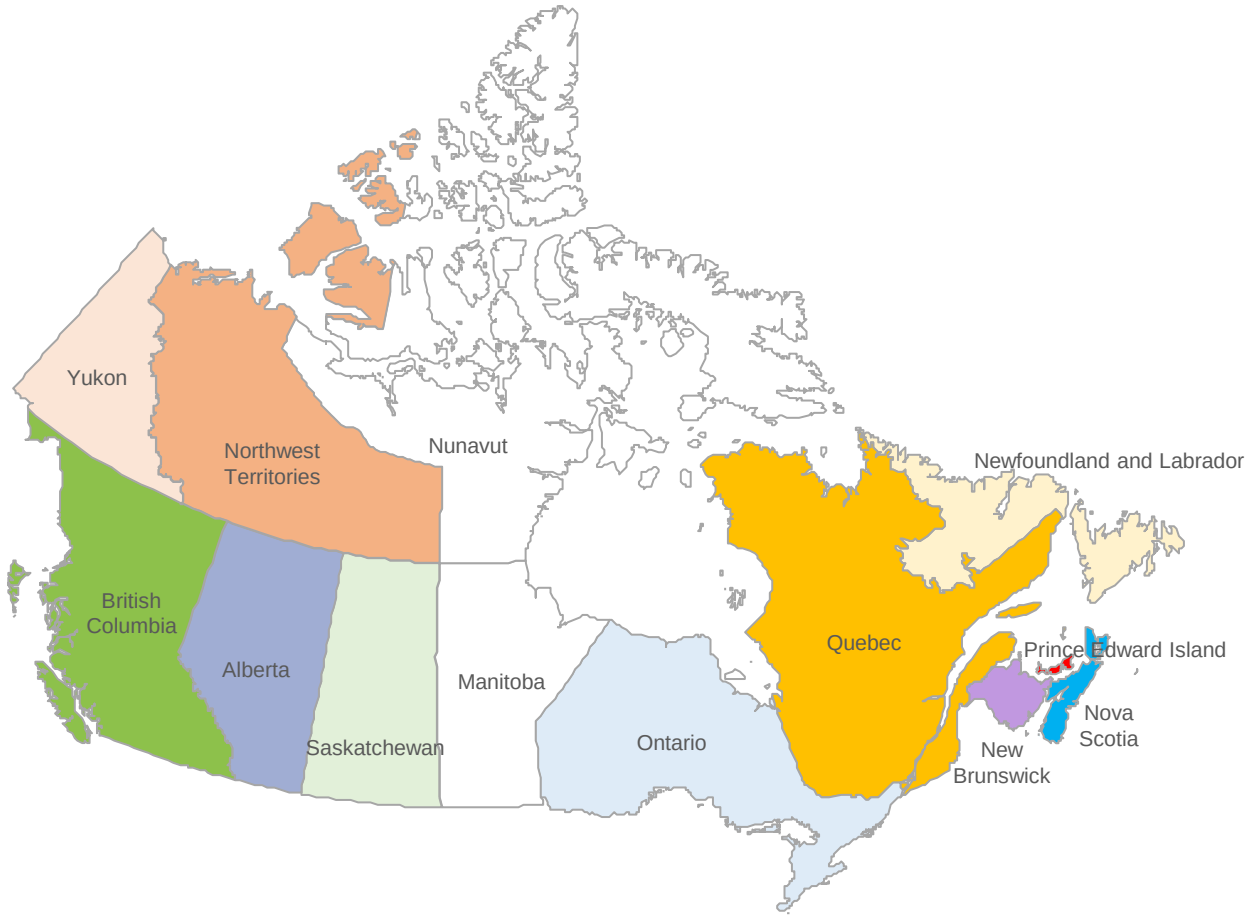
Beer-Sheva and Tel Aviv, Israel; Hamilton, Ontario, Canada; Vicenza, Italy; Buffalo, New York; Porto, Portugal; Chennai, India; Paramus, New Jersey; Barcelona, Spain; and Salford, United Kingdom

Transitioning approach to biosimilar medicines in eight Canadian Provinces and two Territories

- British Columbia[1], Alberta[2], Saskatchewan[3], Ontario[4], Quebec[5], New Brunswick[6], Nova Scotia[7], Newfoundland and Labrador[8], the Yukon[9], the Northwest Territories[10], and the Prince Edward Island[11] 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.

- Biosimilars are now being used to fill 80.9% of all Canadian rituximab prescriptions, 74.8% of all etanercept prescriptions and 67.3% of adalimumab prescriptions.

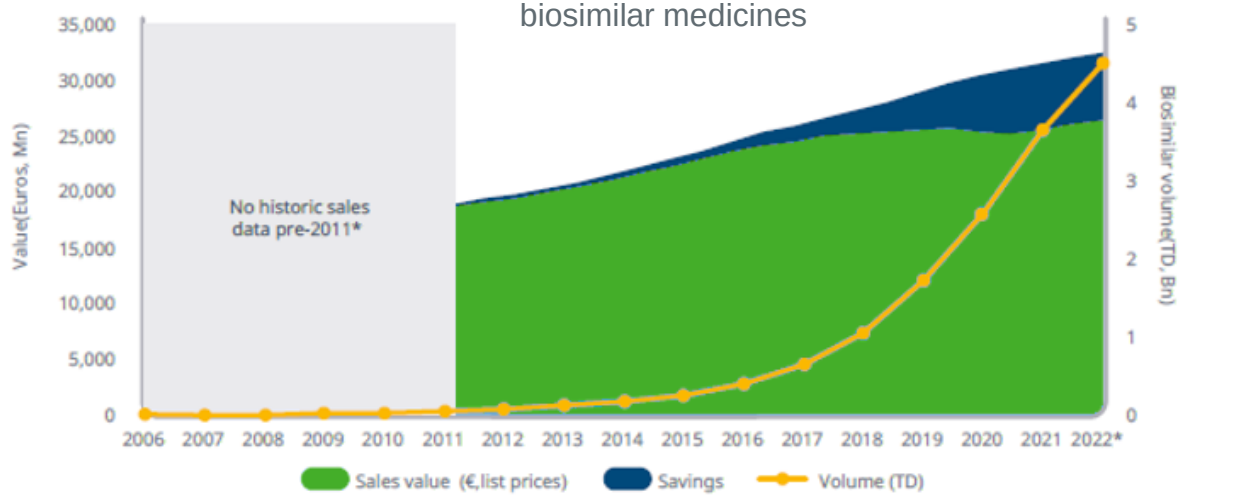


1. British Columbia; 2. Alberta; 3. Saskatchewan; 4. Ontario; 5. Quebec; 6. New Brunswick; 7. Nova Scotia ; 8. Newfoundland and Labrador; 9. Yukon; 10. Northwest Territories ; 11. Prince Edward Island

The total clinical experience with biosimilar medicines exceeded 4.5 billion patient treatment days in Europe

>4.5 Bn

patient days with EU-approved biosimilar medicines



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]

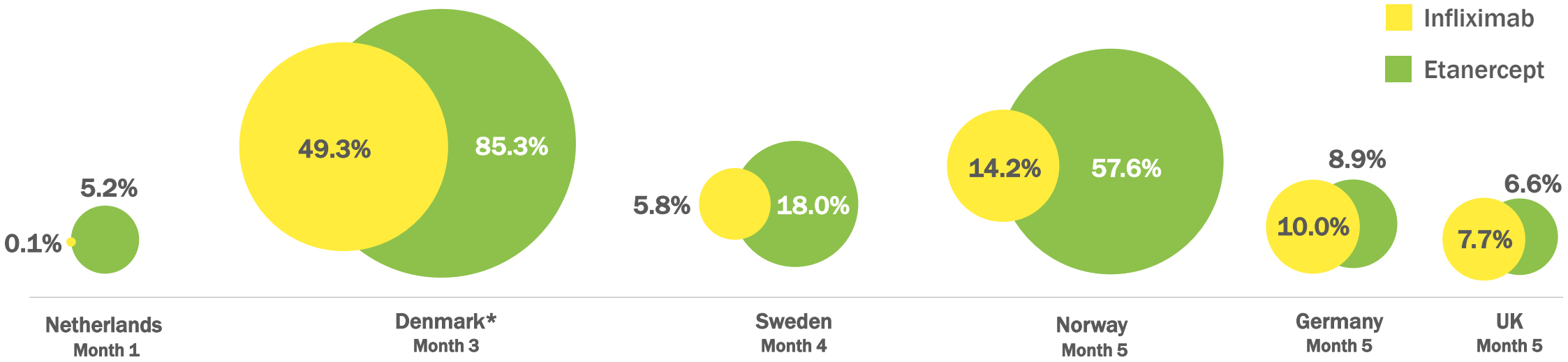
Since 2006, the cumulative patient treatment days for EU approved biosimilar medicines have doubled every ~1.5 years[1]

Reference: 1. . IQVIA report Biosimilar competition in Europe (Dec 2022) Accessed Sept 2023 2. Biosimilars Council https://biosimilarscouncil.org/wp-content/uploads/2021/06/Patient-Days-Infographic-.pdf

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

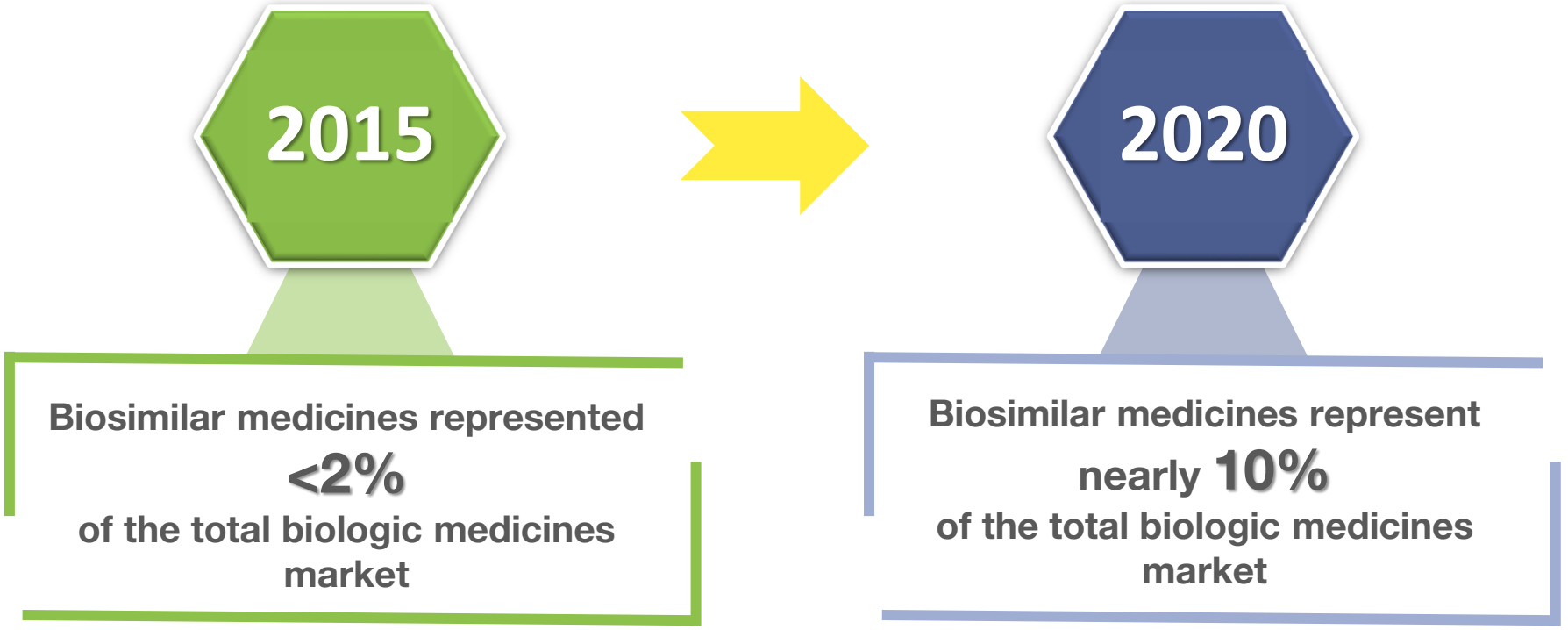


The launch and uptake of multiple biosimilar medicines provides a competitive biologics marketplace

*Denmark data from MIDAS monthly restricted database

Reference: QuintilesIMS. MIDAS July 2016.

In Europe, biosimilars have captured 7% more of the biologics market[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

e.g.: denosumab, aflibercept, ranibizumab

e.g.: darbepoietin

e.g.: insulin aspart, liraglutide

e.g.: cetuximab, daratumumab, ipilimumab, nivolumab, pegaspargase, pembrolizumab, pertuzumab, ramucirumab

e.g.: abatacept,belimumab, certolizumab pegol, interferon beta, golimumab, natalizumab, secukinumab, tocilizumab, ustekinumab

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.

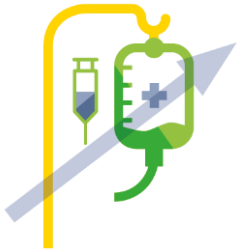
References: 1. Li E, *et al. Drug Des Devel Ther* 2015;9:3247–55; **2.** Kudrin A. Why 2017 Is The Year To Watch Biosimilars. Accessed March 2020.

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[2–6]

Switching from a reference product to a biosimilar medicine is considered **safe** and has become **clinical practice**[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

References: 1. QuintilesIMS Institute for Healthcare Informatics. Delivering on the Potential of Biosimilar Medicines. 2016;
2. European Medicines Agency. Accessed March 2020; **3.** Ministry of Health, Labour and Welfare (MHLW). Accessed March 2020; **4.** Health Canada. Data on file; **5.** Food and Drug Administration. Purple Book. Accessed March 2020; **6.** Australian Register of Therapeutic Goods (ARTG). Accessed March 2020; **7.** Ebbers HC, *et al. Expert Opin Biol Ther.* 2012;12(11):1473–85; **8.** QuintilesIMS MIDAS MTH July 2016.