An introduction to biosimilar medicines

MS nurse pocket guide

The contents of this training were co-created and approved by an international advisory committee of experts in MS nursing and nurse education, and sponsored by Sandoz.

MS, multiple sclerosis.

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Who is this pocket guide for?

This pocket guide is intended to be a brief reference on a number of biosimilar-related topics that multiple sclerosis (MS) nurses can choose from to prepare ahead of, or support during, any given conversation with patients

How and when should you use this guide?

Full review of this guide prior to use during discussions with patients is encouraged

This pocket guide is presented in a single-sided format for digital or printed use

1. **For digital use:** When opened on your laptop or tablet, the left side of the guide contains patient-friendly imagery along with key messages. This provides a visually engaging and easy-to-understand introduction to the topic. The right side of the digital version contains discussion points that you can use to describe concepts to patients in a Q&A format
2. **For printing:** Once printed, fold each page along the center vertical line. This will create a patient-facing side with patient-friendly imagery and key messages, and a rear, nurse-facing side, containing discussion points that you can use to describe concepts to patients in a Q&A format

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A biologic is a medicine that is made from living cells

Figure 1:

Biologic medicines are used to treat many diseases, such as:[1-3]

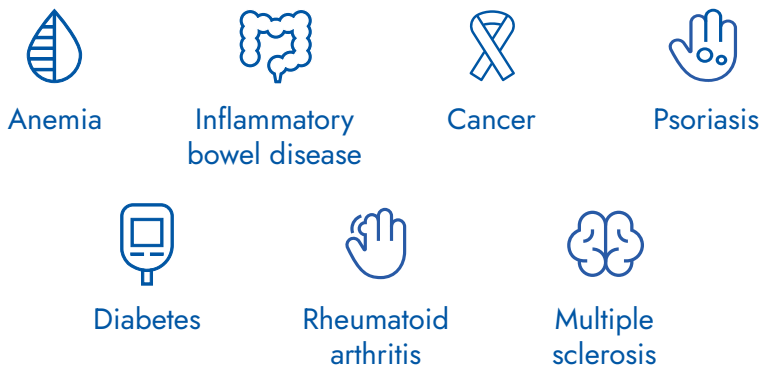
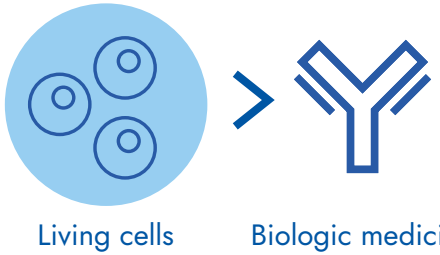


Figure 2:

Biologic medicines (e.g. antibodies) are created using living cells:[1,2,4]



To create a biologic medicine, cells are modified and grown in a carefully controlled setting[4]

Biologic medicines are tailor-made treatments made from living sources to induce a specific treatment effect[6]

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MS nurse discussion points:

Q: What are biologic medicines and how are they made?

1. Biologic medicines are innovative treatments that play an important and increasingly large role in the targeted treatment of a number of life-threatening and disabling disorders, such as diabetes, psoriasis, cancer, MS and arthritis[1–3] *(see Figure 1)*
2. Biologic medicines are not like medicines such as aspirin or paracetamol, which are called small molecule medicines that are made with chemicals and therefore less difficult to characterize than biologics[1,2,4]
3. A biologic medicine is produced by living sources such as cells and tissues, and microorganisms like bacteria or yeast[1,2,4] *(see Figure 2)*
4. Scientists modify living cells that are cultivated under controlled conditions. These cells act like factories, continuously making the medicine, which is then extracted and purified[5]
5. During the manufacturing process, there might be a minor natural variability in the batches of medicine, but it is normal and tightly controlled to maintain the medicine's quality[3-6]
6. One of the reasons biologic medicines are effective is that they are tailor-made to interact with specific targets in the body. This increases the potential that they will have the desired effect against the disease they are designed to treat[6]

MS, multiple sclerosis.

1. US FDA. Biosimilars Basics for Patients. Available at: https://www.fda.gov/drugs/biosimilars/biosimilars-basics-patients. Accessed June 2024; **2.** European Commission. Consensus information paper 2016. What I need to know about biosimilar medicines – information for patients. Available at: https://ec.europa.eu/newsroom/growth/items/419679/en Accessed June 2024; **3.** Greenberg G, Giovannoni G. *Mult Scler Relat Disord* 2023;77:104841; **4.** US FDA. Biological product definition. Available at: https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf. Accessed June 2024; **5.** Medicines for Europe. Biosimilar medicine handbook. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/04/Medicines-for-Europe_BIOSIMILARS_INT_web.pdf. Accessed June 2024; **6.** Zhao L, Ren TH, Wang DD. *Acta Pharmacol Sin* 2012;33:1339–1347.

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A biosimilar medicine is a successor to an already approved biologic medicine

Figure 1:

A biosimilar medicine is developed to be highly similar to its reference biologic medicine: [1]

Reference biologic medicine | Biosimilar medicine

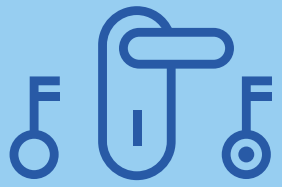
Figure 2:

Biosimilar and reference biologic medicines:[1,2]

- Same active ingredient
- Produced to the same quality standards
- Matching efficacy and comparable safety and immunogenicity

Figure 3:

Patients can expect the same treatment effect when using a reference biologic or biosimilar medicine:[1]



Think of a reference biologic and a biosimilar like an original key and another version that a locksmith makes. Both keys produce the same result: both will fit the same lock and open the same door, even if there are slight differences between the keys

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MS nurse discussion points:

Q: What is a biosimilar medicine?

1. A biosimilar medicine is a biologic that is developed to be highly similar to an existing, approved, and marketed 'reference' biologic medicine[1,2] *(see Figure 1)*
2. A biosimilar medicine has the same active substance, is used for the same illness, and is given the same way, with the same strength and dosage as the reference biologic[1,2] *(see Figure 2)*
3. Biosimilar medicines come into the market once the patent has expired for the reference biologic and are subject to strict approval processes[2,3]
4. A biosimilar medicine provides the same benefits as its reference medicine when treating diseases or medical conditions and have the same treatment risks and benefits[1] *(see Figure 3)*
5. All reference biologics and their biosimilar medicines exhibit a certain degree of inherent natural variability, known as 'microheterogeneity'. Therefore, no two batches of the same biologic from the same manufacturing process at the same site are 100% identical; there is even variability within a single batch[2,4,5,6]

MS, multiple sclerosis.

1. US FDA. Biosimilars Basics for Patients. Available at: https://www.fda.gov/drugs/biosimilars/biosimilars-basics-patients. Accessed June 2024; **2.** European Medicines Agency. Questions and answers on biosimilar medicines (similar biological medicinal products). Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/03/WC500020062.pdf. Accessed June 2024; **3.** US FDA. Biosimilar development review and approval. 2022. Available at: https://www.fda.gov/drugs/biosimilars/review-and-approval. Accessed June 2024; **4.** Kay J. *J Intern Med* 2019;285:693–695; **5.** Planinc A, Dejaegher B, Heyden YV, et al. *Eur J Hosp Pharm* 2017;24:286–292; **6.** Schiestl M, Stangler T, Torella C, et al. *Nat Biotechnol* 2011;29:310–312.

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Biosimilar medicines are different from generic medicines

Figure 1:

Biosimilar medicine
Complex, made from living cells

Generic medicine
Simple, made from chemical substances

Figure 2:

Generics are identical chemical copies of branded medicines, while biosimilars are made from living cells and are highly similar to the reference medicine:[1,2]

Biosimilar medicines[1–3]	Generic medicines[1–3]
Contain the same active ingredient of its reference biologic medicine	Contain the same active ingredient of its branded small molecule medicine
Made from living cells	Made from chemical substances
Complex structure	Simple structure
Complex to manufacture	Easy to manufacture

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MS nurse discussion points:

For all communication points below, see Figure 1 and 2

Q: Why aren't biosimilar medicines simply called generics?

1. Generic medicines are identical copies of branded 'small molecule' medicines[1,2]
2. Generic medicines are made by combining specific chemical ingredients together in known quantities and to recreate the simple molecular structure of the branded small molecule medicine[1,2]
3. Reference biologic and biosimilar medicines are highly complex in comparison to small molecule medicines and cannot be recreated chemically. Biologic medicines must be made using living cells[1,2]
4. Generic and biosimilar medicines are tested and approved for use under different rules that take the above-mentioned differences into account[3]

MS, multiple sclerosis.

1. US FDA. Overview for Health Care Professionals. Available at: https://www.fda.gov/drugs/biosimilars/overview-health-care-professionals. Accessed June 2024; **2.** US FDA. Generic drugs: Questions & Answers. Available at: https://www.fda.gov/drugs/frequently-asked-questions-popular-topics/generic-drugs-questions-answers. Accessed June 2024; **3.** US Food and Drug Administration. Biosimilars Info Sheet. Available at: https://www.fda.gov/media/154912/download. Accessed June 2024.

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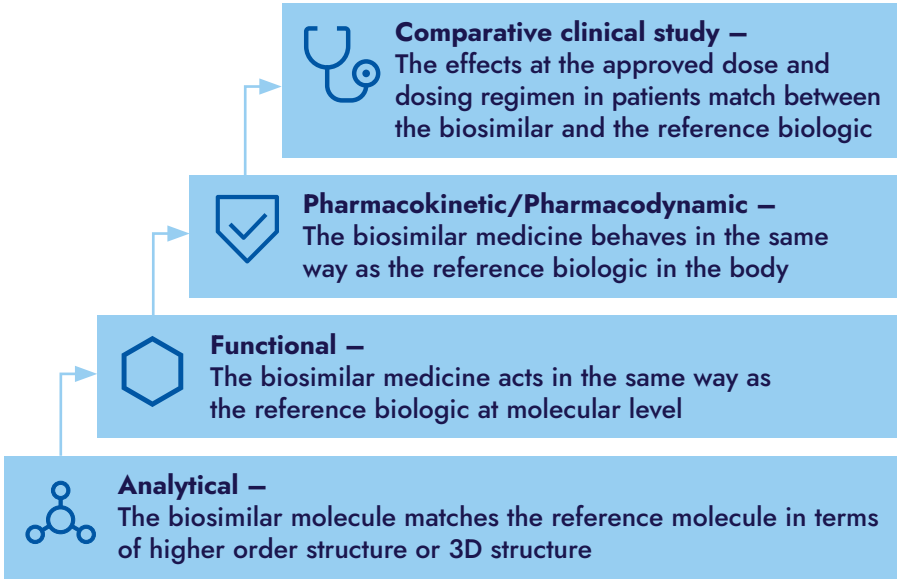
Approving biosimilar medicines is a careful step-by-step process to confirm highly similar efficacy, safety and quality of the reference biologic

When considering development and approval processes, European and US authorities apply the same high standards to all biologic medicines, irrespective of whether they are reference biologics or biosimilars[1,2]

Figure 1:
Similarity is proven by carefully comparing the biosimilar medicine with the reference medicine:[1-3]



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MS nurse discussion points:

Q: How are biosimilar medicines assessed and approved?

1. Biosimilar medicines go through a strict process of evaluation by authorities such as the US Food and Drug Administration (known as the US FDA) or the European Medicines Agency (known as the EMA)[1–3]

Q: Are biosimilar medicines as safe and effective as reference biologics? How is this ensured?

1. Biosimilar medicines are developed to be just as safe and effective as the reference biologics and the studies performed as part of their development process test this by comparing the biosimilar and reference biologic in-depth[1–3] *(see Figure 1)*
2. To ensure that biosimilar medicines provide the same treatment benefits and risks as their reference biologic, stringent biosimilar development guidelines by US FDA/EMA must be followed[2,3]

Q: Are biosimilar medicines monitored?

1. As for all health authority approved medicines, biosimilar medicines are continually monitored to ensure that any clinically important safety information is provided to clinicians in a timely manner[4]

MS, multiple sclerosis; US, United States.

1. US Food and Drug Administration (FDA). Guidance for industry: Scientific considerations in demonstrating biosimilarity to a reference product. 2015. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291128.pdf. Accessed June 2024; **2.** European Commission. Consensus information paper 2016. What I need to know about biosimilar medicines – information for patients. Available at: https://ec.europa.eu/docsroom/documents/26643. Accessed June 2024; **3.** US FDA. Biosimilar development review and approval. 2022. Available at: https://www.fda.gov/drugs/biosimilars/review-and-approval. Accessed June 2024; **4.** US Food and Drug Administration. Medical product safety information. Available at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/default.htm. Accessed June 2024.

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Switching between reference biologics and biosimilar medicines has occurred for many years

Figure 1:

Switching describes replacing one medicine with another one. For biosimilar medicines, switching means that a prescribed reference biologic is changed to its biosimilar medicine, or vice versa:[1,2]

Reference biologic medicine Biosimilar medicine

Switching between reference biologics and biosimilar medicines has taken place for many years across diverse therapeutic areas[3–7]

Based on the latest available evidence, including a large and comprehensive study by the US FDA, switching between a reference biologic and its biosimilar medicine is safe and effective, and the **same treatment effects can be expected[6]**

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MS nurse discussion points:

Q: What is switching?

1. For reference and biosimilar biologic medicines, switching is where one medicine is replaced with another version of that medicine that will have the same treatment outcome[1,2] *(see Figure 1)*
2. Switching may occur if a biosimilar medicine for the reference biologic that you have been treated with becomes available[1,2] *(see Figure 1)*

Q: Can I expect the same treatment effects after switching from my reference biologic to its biosimilar medicine?

1. An extensive review by the FDA found no difference in safety or immunogenicity rates in patients who were switched to or from a biosimilar medicine, compared to those who remained on a reference medicine or biosimilar across various biosimilars and therapeutic areas[6*]

Q: Who decides if a treatment is switched to a biosimilar medicine and why?

1. A treating physician will decide, in partnership with their patient, to switch a treatment from the reference biologic to its biosimilar.[8] There are many reasons why a healthcare system may move to biosimilar medicines, including to support treatment availability and costs, and to support increased access for patients to a medicine[8,9] (see next page for more information)

Q: Will I have any additional side effects after switching?

1. Switching to a biosimilar medicine is not expected to cause any additional side effects, as the efficacy and safety profile of the biosimilar medicine will have been shown to to be highly similar to the reference biologic before its approval for use[1–5]
2. However, it is essential to inform your healthcare provider if you experience any unexpected symptoms while receiving any treatment, whether with a reference or biosimilar biologic medicine

*Please refer to the full publication for further details on study limitations of this meta-analysis.

1. European Medicines Agency. Biosimilars in the EU: Information guide for healthcare professionals. Available at: https://www.ema.europa.eu/en/documents/leaflet/biosimilars-euinformation-guide-healthcare-professionals_en.pdf. Accessed June 2024; **2.** US FDA. 9 Things to Know About Biosimilars and Interchangeable Biosimilars. Available at: https://www.fda.gov/drugs/things-know-about/9-things-know-about-biosimilars-and-interchangeable-biosimilars. Accessed June 2024; **3.** Barbier L, Ebbers HC, Declerck, et al. *Clin Pharmacol Ther* 2020;108:734–755; **4.** Jørgensen KK, Olsen IC, Goll GL, et al. *Lancet* 2017;389:2304–2316; **5.** Cohen HP, Blauvelt A, Rifkin RM, et al. *Drugs* 2018;78:463–478; **6.** Herndon TM, Ausin C, Brahme NN, et al. *PloS One* 2023; 3;18(10):e0292231; **7.** European Specialist Nurses Organisation (ESNO). Switch Management between similar biological medicines. Available at: https://www.esno.org/assets/files/biosimilar-nurses-guideline-final_EN-lo.pdf. Accessed June 2024; **8.** Mysler E, Azevedo VF, Danese S, et al. *Drugs* 2021;81:1859–1879; **9.** Institute of Management Services. Delivering on the promise of biosimilar medicines: The role of functioning competitive markets. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/03/IMS-Institute-Biosimilar-Report-March-2016-FINAL.pdf. Accessed June 2024.

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There are potential economic benefits associated with biosimilar medicines

Figure 1:
Biosimilar medicines may:[1–5]

- Help **more patients access a particular treatment**
- **Support a sustainable healthcare system** for a **wider range of patients**
- Help **healthcare systems save costs by providing more cost-effective treatment** options **without impacting therapeutic outcomes** for patients
- Potentially **decrease wait times for treatment,** which may lead to **improved patient care** and outcomes

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MS nurse discussion points:

Q: Why did my treatment change to a biosimilar medicine? What are the benefits of using a biosimilar?

1. Biosimilar medicines are added to the list of treatments provided by a healthcare system for reasons such as:[1–5] *(see Figure 1)*
   - To widen the number of treatment options available to patients
   - To reduce overall treatment costs as biosimilar medicines are often more cost effective than reference biologics
   - To enhance patient care and outcomes by potentially reducing treatment wait times
2. The aim of a biosimilar is to improve access to medicines and support as many patients as possible[1–5] *(see Figure 1)*
3. In publicly funded healthcare, the aim is to provide safe and effective treatment while minimizing costs for sustainability; so switching to biosimilar medicines when equally safe and effective is common:
   - To help guide decision making regarding switching to a biosimilar medicine, doctors can draw on growing practical, real-world experience with biosimilar medicines (some have been in use for over a decade)[6]
   - The US FDA MedWatch online portal exists to provide doctors with clinically important safety information and reporting serious problems with human medical products for human medical products including biologic medicines[7]

MS, multiple sclerosis.

1. European Medicines Agency. Biosimilars in the EU: Information guide for healthcare professionals. Available at: https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf. Accessed June 2024; **2.** Institute of Management Services. Delivering on the promise of biosimilar medicines: The role of functioning competitive markets. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/03/IMS-Institute-Biosimilar-Report-March-2016-FINAL.pdf. Accessed June 2024; **3.** US FDA. Biosimilar Basics. Available at: https://www.fda.gov/media/166369/download?attachment. Accessed June 2024; **4.** Biosimilar Medicines Group. Biosimilar Medicines Group handbook 2016. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/04/Medicines-for-Europe_BIOSIMILARS_INT_web.pdf. Accessed June 2024; **5.** Simon-Kucher & Partners. Payers' price & market access policies supporting a sustainable biosimilar medicines market. PowerPoint Presentation. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/09/Simon-Kucher-2016-Policy-requirements-for-a-sustainable-biosimilar-market-FINAL-report_for-publication2.pdf. Accessed June 2024; **6.** Sagi S, Anjaneya P, Kalsekaar S, et al. *Drug Saf* 2023; 46(12):1391-1404; **7.** US FDA. Medical product safety information. Available at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/default.htm. Accessed June 2024.

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Biosimilar medicines have benefitted many patients worldwide

Biosimilar medicines have helped many patients and healthcare systems globally across several therapy areas

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MS nurse discussion points:

Q: Are biosimilar medicines common treatment options?

1. Biosimilar medicines have had a positive impact worldwide, increasing treatment availability and accessibility to patients. For example, in different countries in Europe, biosimilars have increased treatment availability and flexibility in cancer care as well as in the management of inflammatory rheumatic diseases[1–3]
2. The introduction of biosimilars in Europe and the US has led to higher usage of biologic medicines, such as those used for growth hormone deficiency treatment and IBD. Greater access to treatment has allowed for reduced healthcare costs, early treatment, greater adherence, and increased competition[4-6]
3. A US hospital study in adult patients with IBD showed that, following the introduction of biosimilar infliximab, 97% of eligible patients successfully switched and, of those, 83% were still using the biosimilar 12–15 months after the switch[7]
4. In the US, biosimilar filgrastim achieved significant adoption during the first 3 years of entering the market, accounting for approximately 50% of filgrastim claims in Medicare and around 39% in Medicaid populations[8]
5. A large and comprehensive study by the US FDA for 21 different biosimilars demonstrated that switching between a reference biologic and its biosimilar medicine is safe and effective, and that the same treatment effects can be expected[9]

IBD, inflammatory bowel disease; MS, multiple sclerosis; US, United States.

1. Institute of Management Services (IMS). Delivering on the Promise of Biosimilar Medicines: The Role of Functioning Competitive Markets. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/03/IMS-Institute-Biosimilar-Report-March-2016-FINAL.pdf. Accessed June 2024; **2.** European Specialist Nurses Organisation (ESNO). Switch Management between similar biological medicines. Available at: https://www.esno.org/assets/files/biosimilar-nurses-guideline-final_EN-lo.pdf. Accessed June 2024; **3.** Hörbrand F, Schuch F, Bleß HH, et al. PHARAO study: Drug treatment of inflammatory rheumatic diseases: Guideline-conform treatment with biologics follows availability of biosimilars. *Z Rheumatol* 2022;10.1007/s00393-022-01259-5; **4.** National Institute for Health and Care Excellence (NICE) UK. 2021. Available at: https://www.nice.org.uk/news/articles/nice-recommends-several-treatment-options-to-help-thousands-with-moderate-rheumatoid-arthritis. Accessed June 2024; **5.** IQVIA: 15+ Years of Biosimilar Experience November 2022. Available at: https://secure.constellation.iqvia.com/OmintropeReport. Accessed June 2024; **6.** D'Amico F, Peyrin-Biroulet L, Danese S. *J Clin Med* 2024;13(11):3069. **7.** Bhat S, Altajar S, Shankar, et al. *J Manag Care Spec Pharm* 2020;26(4):410–416; **8.** Qian J. *J Manag Care Spec Pharm* 2021;27(5):660–666; **9.** Herndon TM, Ausin C, Brahme NN, et al. *PloS One* 2023; 3;18(10):e0292231.

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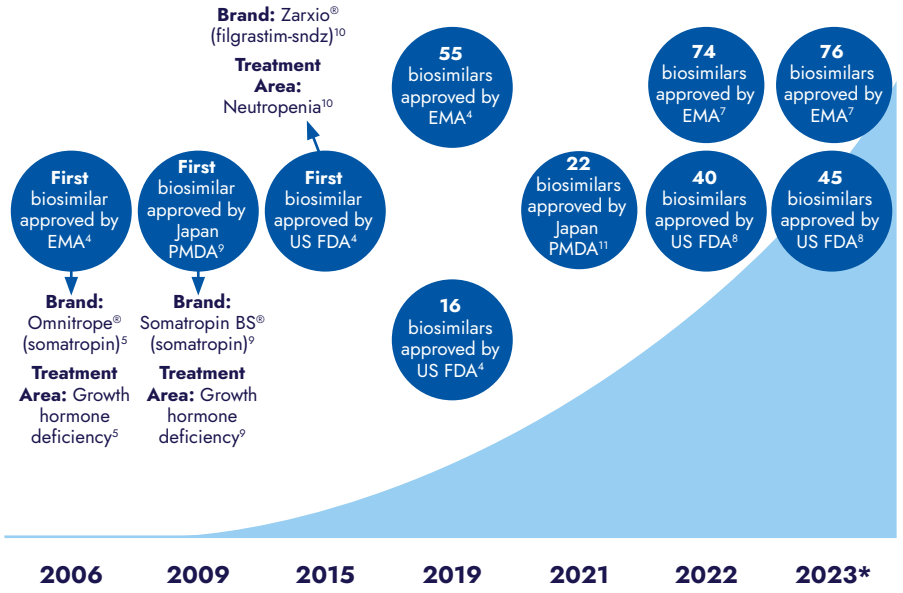
Biosimilar medicines have supported healthcare outcomes since 2006

Figure 1:

A brief history of biosimilar medicine approvals worldwide:



With 76 approved in Europe and 45 in the US*, biosimilar medicines continue to expand treatment options worldwide across diverse therapy areas

*As of January 2024.

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MS nurse discussion points:

For all communication points below, see Figure 1

Q: Are biosimilar medicines a new treatment option?

1. Biosimilar medicines have been in use for over 15 years for different diseases such as rheumatoid arthritis, ulcerative colitis, some cancers, diabetes and osteoporosis. Biosimilar medicines are also moving into new diseases, including MS[1–4]
2. The first biosimilar medicine, somatropin, was approved by the EMA in 2006 for the treatment of children with growth failure[4,5]
3. Since its approval, >40,000 patients have been treated with, and have benefitted from, biosimilar somatropin for 107 million days[6]
4. As of 2023, 76 biosimilar medicines have been approved in Europe[7] and 45 in the US[8] for different conditions*

*As of January 2024.

EMA, European Medicines Agency; FDA, Food and Drug Administration; MS, multiple sclerosis; PMDA, Pharmaceuticals and Medical Devices Agency; US, United States.

1. European Commission. Consensus information paper 2016. What I need to know about biosimilar medicines – information for patients. Available at: https://ec.europa.eu/docsroom/documents/26643. Accessed June 2024; **2.** Institute of Management Services. Delivering on the promise of biosimilar medicines: The role of functioning competitive markets. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2016/03/IMS-Institute-Biosimilar-Report-March-2016-FINAL.pdf. Accessed June 2024; **3.** Tyruko®. PI. 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761322s000lbl.pdf. Accessed January 2024; **4.** Gherghescu I, Delgado-Charro MB. *Pharmaceutics* 2021;13(1):48; **5.** European Medicines Agency. Omnitrope® (somatropin). Summary of Product Characteristics, 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/omnitrope-epar-product-information_en.pdf. Accessed June 2024; **6.** Saenger P. *Drug Des Devel Ther* 2017;11:1505–1507; **7.** Generics and Biosimilar Initiative. 2023. Available at: https://gabionline.net/biosimilars/general/. Accessed June 2024; **8.** US Food and Drug Administration. Biosimilar Product Information. 2023. Available at: https://www.fda.gov/drugs/biosimilars/biosimilar-product-information. Accessed June 2024; **9.** Farhat F, Torres A, de Lima Lopes G, et al. *Oncologist* 2018;23(3):346–352; **10.** Zarxio®. Prescribing Information, 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs label/2021/125553s023lbl.pdf. Accessed June 2024; **11.** Kang HN, Thorpe R, Knezevic I, et al. *Biologicals* 2020;65:1–9.

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