

What is a Biosimilar Medicine?



NHS England and NHS Improvement



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The following organisations, listed alphabetically, have partnered with NHS England in developing this document.

- Association of the British Pharmaceutical Industry (ABPI)
- BioIndustry Association (BIA)
- British Biosimilars Association (BBA)
- Medicines and Healthcare Products Regulatory Agency (MHRA)
- The National Institute for Health and Care Excellence (NICE)
- Royal Pharmaceutical Society (RPS)
- National Rheumatoid Arthritis Society (NRAS)
- NHS England Biosimilars Programme Board

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- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

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1 Executive Summary

The aim of this document is to provide an update for key clinical and non-clinical stakeholders about the role of biosimilar medicines in the NHS in England and to support the safe, effective and consistent use of all biological medicines, including biosimilar medicines, to the benefit of patients.

As original biological medicines lose their patent protection, biosimilar medicines are becoming available across different therapeutic areas. There are currently 15 'reference' (or 'originator') biological medicines that have biosimilars approved for use in the UK, as well as many in development. As the biosimilar market develops, increased competition between biological medicines has the potential to deliver significant savings to the NHS of at least **£400m to £500m per year by 2020/21** through increased uptake of the **best value biologic medicines**, including biosimilars.¹

Actions set out in the NHS Commissioning Framework for Biological Medicines (including biosimilar medicines) will help the NHS to maximise the value for patients from the amount it spends on these medicines and enable much needed headroom for funding innovative treatments and/or improvements in pathways of care.²

Key messages:

- Biological medicines are medicines that are made or derived from a biological source and as such are complex, with inherent variability in their structure. ([see 3.1](#))
- A biosimilar medicine is a biological medicine which has been shown not to have any clinically meaningful differences from the reference medicine in terms of quality, biological activity, safety, efficacy and immunogenicity³. ([see 3.2](#))
- A biosimilar medicine is not the same as a generic medicine, which contains simpler molecular structures. Generic medicines contain active ingredients that are identical to the originator medicine. ([see 3.2](#))
- For a biosimilar medicine to be approved, regulatory requirements include comprehensive comparability studies with the reference biological medicine. If a biosimilar is highly similar to a reference medicine and has comparable safety and efficacy in one indication, safety and efficacy data may be extrapolated to other indications already approved for the reference medicine, if scientifically justified. This avoids the unnecessary repetition of clinical trials. ([see 3.3.1](#))
- Where NICE has already recommended the reference biological medicine, the same guidance will normally apply to a biosimilar of the reference medicine. ([see 3.3.2](#))
- Biosimilar medicines are considered to be highly similar and therapeutically equivalent to the reference biological medicine. As a result, the prescriber can switch a patient from the reference biological medicine to its biosimilar.⁴ ([see 4.5](#))

- The decision to prescribe a biological medicine for an individual patient, whether a reference or biosimilar medicine (or to change between the two), rests with the responsible prescriber in consultation with the patient; in line with the principles of shared decision making. This should be in accordance with the approved indications on the **summary of product characteristics (SmPC)** and ideally be part of a biological medicines review. [\(see 4.3\)](#)
- Biological medicines, including biosimilars, should be prescribed by their brand name and not by the **international non-proprietary name (INN)**, in line with MHRA guidelines and to support ongoing pharmacovigilance. [\(see 4.6\)](#)
- NHS England, NHS Improvement and NHS Clinical Commissioners through the Commissioning Framework for biological medicines (including biosimilars)⁵ support the appropriate use of the best value biological medicine which will drive greater competition to release cost efficiencies to support the treatment of an increasing number of patients with biological medicines and the uptake of new and innovative medicines.

Key terms are highlighted in **grey** throughout the document and are explained in more detail in the [glossary](#).

2 Background

Biological medicines are well established in clinical practice and offer effective and in many cases vital medicines for acute and chronic conditions including neutropenia, different types of cancers, diabetes, a wide range of inflammatory and autoimmune diseases such as arthritis, psoriasis, as well as enzyme or hormone deficiencies. Where patents expire for individual biological medicines, **biosimilar medicines** are being introduced to provide additional treatment options for patients and the NHS.

Q: How long have they been around?

A: The first biosimilars, both somatropins, received their marketing authorisation from the European Commission in 2006. By **November** 2018, biosimilars to 15 reference medicines (**35** biosimilar molecules marketed as **53** brands) have been authorised for use by patients across Europe. But this list continues to grow, and the latest information can be found on the EMA website, a link is provided in 5.2 *Where can additional information and support be found?*

Biosimilar medicines have been used in clinical practice for over 12 years as treatments for growth hormone replacement, neutropenia and anaemia related to chronic renal failure or cancer. Since 2013, the European Commission, on the advice of the European Medicines Agency, has authorised biosimilar medicines for infliximab, etanercept, rituximab, adalimumab, trastuzumab, bevacizumab, enoxaparin, insulin glargine, insulin lispro, teriparatide, follitropin alfa and pegfilgrastim, to add to those already approved; somatropin, filgrastim and epoetin alfa.

3 Key facts

3.1 What is a biological medicine?

Biological medicines are derived from living cells or organisms and consist of large, highly complex molecular entities which may be difficult to characterise. Due to the variability of the biological system and the manufacturing process, biological medicines may show a certain degree of variation, even between batches of the same product.⁶

3.2 What is a biosimilar medicine?

A biosimilar medicine is a biological medicine that is developed to be highly similar and clinically equivalent to an existing medicine.⁷ A biosimilar contains a version of an active substance of an already approved biological medicine, which is referred to as the 'reference medicine'. Similarity to the reference medicine must be established based on a comprehensive biosimilar comparability exercise, such that they do not have any clinically meaningful differences from the reference medicine in terms of quality, biological activity, safety, efficacy and immunogenicity.^{8,9} **Comparability** is a well-established concept, used to evaluate manufacturing changes in biological medicines ([see 3.3](#)).

If a biosimilar is highly similar to the reference medicine and has comparable safety and efficacy in one indication, safety and efficacy data may be **extrapolated** to other indications already approved for the reference medicine, if scientifically justified.¹⁰ This avoids unnecessary repetition of clinical trials.¹¹

Biosimilar medicines are not the same as generic medicines, which contain simpler chemical structures and are identical, in terms of molecular structure, to their reference drugs.¹²

3.3 How are biosimilar medicines authorised for use?

3.3.1 European licensing

In the European Union, Marketing Authorisation applications for **biotechnology-derived medicines**, including biosimilar medicines, are by law reviewed centrally by the European Medicines Agency (EMA).¹³ The resulting marketing authorisation, issued via a decision by the European Commission, is valid in all EU Member States.¹⁴

Biosimilar medicines require distinct regulatory pathways from those applied to generic medicines as they are not exact replicates of the originator (reference) medicine. The simplified regulatory approval process used for generic medicines is not sufficient to demonstrate similarity for biological medicines, due to their complexity.¹⁵

In 2003, the EU adopted a specific regulatory pathway that provides a robust regulatory process through overarching¹⁶, quality¹⁷, non-clinical and clinical¹⁸, and product class-specific¹⁹ scientific guidelines for biosimilar medicines. The main part of the evaluation is a detailed head-to-head comparison of the biosimilar medicine with its reference medicine to show that there are no clinically significant differences between them.²⁰ The biosimilar pathway does not seek to demonstrate safety and efficacy for each

indication of the biosimilar medicine, as this is done by reference to the originator product, which has already satisfied these requirements.²¹

Depending on the evidence provided for regulatory assessment of the biosimilar medicine, it will typically have all of the therapeutic indications established for the reference medicine. Although there may not be comparative clinical data (phase III studies) in all of these indications for a given biosimilar, the data package submitted when considered in totality must provide sufficient assurance for the EMA to allow **extrapolation** of the biosimilarity assessment to additional indications. Extrapolation of indications is not automatically awarded to the biosimilar, but must be scientifically justified. Once a product has been authorised as a biosimilar by the regulators, it should be considered by the prescriber as therapeutically equivalent in its authorised indications.

Q: How do biological medicines change?

A: Biological medicines change in ways that chemically-manufactured medicines don't. You may hear terms like batch to batch variability, manufacturing change and biosimilarity, and it is important to understand what each means. For details, please see *4.1 Glossary* and *5.2 Where can additional information and support be found?*

All biological medicines may exhibit batch to batch variability which is controlled and maintained within defined and approved limits. Manufacturing changes can occur in both originator biological medicines and biosimilar medicines. These changes are evaluated using a comparability exercise and assessed by the regulator to ensure that any changes do not impact the quality, safety and efficacy of biological medicines. The scientific basis for the biosimilar regulatory pathway relies on that used for **manufacturing changes**.²²

Since the approval of the first biosimilar (Omnitrope®, a somatropin biosimilar to Genotropin®) in 2006, until November of 2018, 35 biosimilar medicines have been authorised under 53 brand names for 15 molecules (somatropin, filgrastim, epoetin alfa, infliximab, etanercept, rituximab, adalimumab, trastuzumab, bevacizumab, enoxaparin, teriparatide, follitropin alfa, pegfilgrastim, insulin glargine and insulin lispro).²³ Once authorised by the European Commission, biosimilars are subject to the same level of post-authorisation regulatory scrutiny as reference products and will pursue their own development (e.g. new indications) and manufacturing changes as any other biological medicine.

3.3.2 Do biosimilars require a health technology assessment?

In England, NICE produced a position paper on biosimilar medicines in 2015.²⁴ NICE will consider biosimilar medicines notified to it by the National Institute for Health Research Horizon Scanning Centre for referral to the Technology Appraisal topic selection process.

If appraised, biosimilars will usually form part of a Multiple Technology Appraisal (MTA) alongside their reference products, in the indication under consideration.

The Department of Health and Social Care in England has confirmed that a technology appraisal remit referred to NICE enables NICE to decide to apply the same remit, and the resulting guidance, to relevant licensed biosimilar products which subsequently

appear on the market.²⁵ Therefore, where NICE has already recommended the reference medicine, that same guidance is likely to apply to the biosimilar medicine.

There may be some occasions where a review of the evidence for the biosimilar medicine is deemed necessary, and in that case, NICE will consider producing a quality-assured summary of the evidence via an Evidence Summary²⁶. Evidence Summaries are not formal NICE guidance and so do not make recommendations.

The decision regarding the choice of biosimilar or reference biological medicine for an individual patient rests with the responsible prescriber in consultation with the patient.²⁷

NICE technology appraisal guidance often recommends treatment with the least expensive drug where there are a number of choices available, taking into account for example administration costs, dosages, mode of administration and treatment schedules.

4 Key considerations for the NHS

4.1 Why should biosimilar medicines be used in the NHS?

The NHS use of medicines has increased significantly due to a range of factors such as changing demographics and new treatments becoming available. The NHS drugs bill is currently £15.5 billion a year and this has increased by one-third since 2010/11 and the cost of medicines used in hospitals has doubled in the last six years. The document 'Next Steps on the NHS Five Year Forward View' and 'Long Term Plan' makes clear that the NHS must take action to maximise the value it derives for patients from the money it spends on medicines.

Biosimilar medicines are more challenging and expensive to develop than generic medicines.²⁸ Whilst they may not offer the same percentage of price reductions as traditional generic medicines, nevertheless, there are significant savings associated with increased competition between biological medicines, including biosimilar medicines.

Competition between different biological medicines, including biosimilar medicines, creates increased choice for patients and clinicians, and enhanced value propositions for individual medicines (such as improved devices, patient services or formulations). When biosimilar medicines have entered the market, the increasing competition enables significant savings to be realised.

The biological medicines market will only increase in complexity in the coming years, as more biological medicines lose patent protection and additional biosimilar medicines come to market. It is important that the NHS continues to monitor and drive action for adopting these biosimilar medicines.

4.2 What considerations should inform a purchasing decision?

Biosimilar medicines are approved to be therapeutic equivalents to the reference medicine, as they have to establish that they are just as safe and effective as the

reference medicine.²⁹ As with any biological medicine, the biosimilar medicine will have details of its licensed indications included in the British National Formulary.

NHS procurement of biological medicines takes place through national and regional procurement processes. The subsequent use of best value biological medicines in the NHS requires a number of key questions to be considered:

- 1) Has due consideration been given to the outcomes of the Commercial Medicines Unit contracting processes in collaboration with the regional pharmacy procurement lead?
- 2) Has appropriate local stakeholder engagement, with key clinicians, nurses, pharmacy staff and patient groups, taken place?
- 3) Have individual patients been appropriately consulted and informed of any proposed changes to their treatment and have any concerns been properly addressed by their clinical team?
- 4) Have the relevant commissioners been made aware of the local implementation plan and timeline for delivery?
- 5) What product specific issues need to be considered? For example:
 - a) Does the biosimilar have the key indications for treatment as part of its licence?
 - b) Will sufficient support be available for patients prescribed the biosimilar?
 - c) What is the route of administration of the product?
- 6) Is there enough resource allocated within the local hospital to support the introduction of the biosimilar?

Further information on NHS procurement and commissioning of best value biological medicines can be found in the NHS Commissioning Framework for Biological Medicines (including biosimilar medicines). ([see 5.2](#))

4.3 How should treatment decisions be made?

The role of the prescriber in treating patients with these complex medicines is of fundamental importance.

The decision to prescribe a biological medicine for an individual patient, whether a reference or biosimilar, or to change between the two, rests with the responsible prescriber in consultation with the patient, in line with the principles of shared decision making. This should be in accordance with the approved indications on the summary of product characteristic and ideally be part of a biological medicines review.

Prescribers should use all available relevant evidence to guide decisions about the care of an individual patient with the initial selection of the most appropriate molecule based on clinical considerations.

Subsequently, prescribers should consider the value propositions offered by different products, including cost and licensed indications, as well as other factors relevant to the use of the product and likely clinical outcomes for each patient.

Further guidance and key contacts for patients looking for information on biological medicines (including biosimilars) can be found in section [5.2.3](#) and [5.2.4](#).

4.4 Is substitution permitted?

Substitution; defined here as the practice of dispensing one medicine instead of another equivalent medicine at the pharmacy level without consulting the prescriber,²⁹ is not permitted for biological medicines, including biosimilars.

In line with MHRA guidance all biological medicines (including biosimilars) should be prescribed by brand name.³⁰

As biosimilar medicines often use the same international non-proprietary name (INN) as their reference product, an important way to ensure substitution does not take place is through brand name prescribing.³¹ Brand name prescribing should be adhered to by all prescribers of biological medicines, including biosimilars, and is in line with recommendations and advice from MHRA and NICE, as well as being enshrined in EU law.

4.5 Can a patient already established on a reference biological medicine be switched to a biosimilar medicine?

Yes, patients established on a reference biological medicine can be switched to a biosimilar medicine at the discretion of the prescriber in consultation with the patient, with appropriate monitoring in place. There is also growing practical NHS experience that demonstrates the safety and efficacy of biosimilars in clinical practice.

Biosimilar products are considered to be **interchangeable** with their reference product; which means a prescriber can choose the biosimilar medicine over the reference product (or *vice versa*) and expect to achieve the same clinical effect (therapeutic equivalence)³². This decision rests with the prescriber in consultation with the patient in line with the principles of shared decision making.

Guidance across some EU Member States currently recommends that switching between a reference product and its biosimilar (and indeed amongst biosimilar medicines) should be managed at the discretion of the individual prescriber in partnership with the patient, with appropriate monitoring in place.^{33,34} Note that there is only limited real-world evidence to support switching between different biosimilar products at present. Substitution is not permitted for biological medicines, including biosimilars. ([see 4.4](#))

Evolving evidence and treatment guidance should be made available to patients and prescribers to support them in their decision-making. Good practice guidance can be found in [section 5.2](#)

4.6 What is important about monitoring biological medicines, including biosimilar medicines?

4.6.1 Pharmacovigilance

Q: Where can I find further information on safety of biological medicines?

A: MHRA and the EMA provide more explanations on how medicines safety is monitored across Europe. The MHRA Drug Safety Updates are a core resource. It is worth noting that by mid-2018, no safety signals different to the reference medicine have been identified for biosimilars. Please see 5.2 *Where can additional information and support be found?*

All medicines in Europe are thoroughly assessed for quality, safety and efficacy before receiving regulatory approval. Once on the market, their safety profile and the balance of benefits to risks is continuously monitored, through a set of processes called pharmacovigilance. In the UK, reports of suspected side effects to medicines should be reported to the Yellow Card scheme³⁵ which is operated by MHRA. Sometimes pharmacovigilance for biosimilar medicines can include the use of Registries. These gather data on the safety and effectiveness of the medicine in clinical practice.³⁶

4.6.2 Recording brand and batch number and reporting suspected adverse reactions (ADRs)

Suspected adverse drug reactions should be reported to MHRA through the [Yellow Card Reporting Scheme](#). MHRA requests that suspected ADRs to any biological medicine should include the brand name and specific batch number on any ADR report³⁷. MHRA also asks that brand name and batch number is provided to patients and carers when the product is administered, to help them report an issue more accurately.³⁸ If brand name or batch number is not available to the reporter, the suspected ADR should still be reported using the INN.

An inability to attribute any safety concerns to the correct product, manufacturer and batch could prevent a root-cause determination and may put patients at risk.³⁹

EU pharmacovigilance legislation additionally mandates that any medicine with a new active substance and all biological medicines, including biosimilar medicines, approved after 1 January 2011, should carry a black inverted triangle (▼) in their labelling for at least five years. This denotes that the medicine, as a new product, is being monitored particularly closely and is subject to so called 'additional monitoring'. The black triangle is intended to encourage both prescribers and patients to record and report suspected adverse drug reactions (ADR)⁴⁰ in line with the collection requirements set out in the commissioning framework.

4.6.3 How can a healthcare professional improve pharmacovigilance?

- Ensure that the brand name and batch number are recorded at all levels, including on a prescription, at the point of dispensing and when it is administered to the patient – this includes written and electronic records
- Ensure that the patient is informed and given written information on which brand and batch they have been administered
- When reporting suspected ADRs to the Yellow Card Scheme, always include the brand and batch name in the report.

Adapted from EMA guide: Biosimilars in the EU, information to guide for HCPs

4.6.4 Registries

For some medicines, there is a regulatory requirement for manufacturers to perform post-authorisation safety studies, or other forms of additional safety and effectiveness surveillance. This can include Patient Registries, which are organised systems that use observational methods to collect uniform data over an extended period of time on a population defined by a particular disease, condition, or exposure. Patient Registries are often used for biological medicines, including many biosimilar medicines. MHRA encourages the collection of data through established registries, if possible.

The EMA has set up an inventory⁴¹ of patient registries, which aims to provide a convenient way to access the information available as it is collected over time.

5 Appendices

5.1 Glossary

A glossary of key terms associated with biosimilar medicines has been included for ease of reference.

- **Active substance:** an active ingredient or molecule which goes into a specific medicine and which provides this medicine with properties for treating or preventing one or several specific disease(s).⁴²
- **Batch to batch variability:** Because biological medicines, including biosimilars, are derived from living organisms and produced using complex manufacturing processes, there is intrinsic variability from batch to batch. This variation is kept within strict acceptable limits, which is monitored by the manufacturer and approved by the regulator, known as 'release specifications'.
- **Best value biologic:** A biological medicine (reference or biosimilar) which can deliver measurable improvement in patient outcomes compared to a biological alternative while maintaining an affordable medicines bill⁴³
- **Biological medicine:** a medicine that contains one or more active substances made by or derived from a biological source. Some of them may be present in the human body and examples include proteins such as insulin and growth hormone. Active substances in biological medicines are larger and more complex than those of non-biological medicines.⁴⁴
- **Biosimilarity:** Assessment of a biological product which has been developed to be highly similar to the reference biological medicine. It must be shown to have highly similar key characteristics of the molecular structure and biological activity, and will be expected to have similar function and clinical outcome. Any differences will be expected to have no meaningful clinical impact on the safety and efficacy of the medicine for patients.
- **Biosimilar medicine:** a biological medicine that is developed to be highly similar and clinically equivalent (in terms of quality, safety and efficacy) to an existing biological medicine that has already been authorised in the European Union, (known as the reference biological medicine or originator medicine). Biosimilar medicines should be considered to be therapeutically equivalent to the reference medicine within their authorised indications.⁴⁵
- **Biotechnology:** any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use. An example is the reproduction of human hormones like insulin.⁴⁶
- **Cell line:** a well-established, living system of cultured (grown in a laboratory) cells that will continue to grow and produce new cells indefinitely, so long as the cells receive nourishment and have space to develop.⁴⁷
- **Extrapolation of indications:** the decision whether to extend the efficacy and safety data from an indication (a medical condition, disorder or disease) for which the biosimilar has been clinically tested to other conditions for which the branded product is approved, is known as 'extrapolation'.⁴⁸

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The decision to extrapolate is based on the entire data package submitted i.e. European Public Assessment Reports (EPAR), of which the selected clinical studies are only part. Extrapolation then follows if the totality of evidence provides assurance. Much of the data in the EPAR is not clinical patient data but does provide assurance in the other indications to which the product is intended to be extrapolated.

- **Immunogenicity:** The body's immune response to a biological medicine which may result in the loss of effectiveness of that drug over time or in rare cases cause a serious adverse reaction.
- **International Non-proprietary Name (INN):** the unique name which identifies pharmaceutical substances or active pharmaceutical ingredients. Also known as a 'generic' name.
- **Interchangeable:** refers to the possibility of the prescriber choosing one medicine over another that is expected to have the same clinical effect (therapeutic equivalence). This could mean switching a reference product with a biosimilar (or *vice versa*).⁴⁹
- **Manufacturing change:** during the commercial lifecycle of all biological medicines, planned changes occur to the manufacturing process, generally minor (such as a change in filter supplier) but sometimes substantial (such as a new manufacturing site). The manufacturer must ensure the process is controlled and the variability remains within release specifications approved by the regulatory authority. The assessment for any manufacturing change is done via a comparability exercise, informed by the historical manufacturing, non-clinical and clinical data available to the manufacturer. Depending on the scale of the change and the potential impact to the product, the regulator may ask for additional analytical data, non-clinical and clinical data, but the aim is to ask only for what is needed to make an assessment.
- **Molecule:** the smallest particle of a substance that has all of the physical and chemical properties of that substance. Molecules comprise two or more atoms held together by strong chemical bonds. If they contain more than one atom, the atoms can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins, can be made up of many thousands of atoms.⁵⁰
- **Pharmacovigilance:** science and safety control procedures to which medicines are subject before, during and after their approval by regulatory authorities with the aim of detecting, assessing and understanding the benefit: risk profile of a medicinal product.⁵¹
- **Prescriber:** a registered health professional with authority under [The Human Medicines Regulations 2012](#) to issue a prescription for a patient
- **'Reference' or 'Originator' product:** a medicinal product which has been granted a marketing authorisation by a Member State or by the European Commission on the basis of submitted quality, pre-clinical and clinical data, to which the application for marketing authorisation for a generic or a biosimilar product refers.⁵²
- **Shared decision making:** a process in which healthcare professionals and patients work together to select tests, treatments, management or support packages, based on clinical evidence and the patient's informed preferences. It involves the provision of evidence-based information about options, outcomes and uncertainties, together with

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decision support counselling and a system for recording and implementing patients' informed preferences.⁵³

- **Substitution:** the practice of dispensing one medicine instead of another equivalent medicine at the pharmacy level without consulting the prescriber. Substitution is not permitted for biological medicines, including biosimilars.
- **Summary of Product Characteristics (SmPC):** A legal document required by law as part of the approval process for each medicine. It is a guide for healthcare professionals on how to use the medicine and is updated as new data emerge throughout the life of the product.⁵⁴
- **Switching:** Decision by the treating physician to exchange one medicine for another medicine with the same therapeutic intent in patients who are undergoing treatment.

5.2 Where can additional information and support be found?

5.2.1 Key reading

#	Document Name	Publication Date	Publication Organisation
1	Guideline on similar biological medicinal products	23-Oct-14	European Medicines Agency
2	Good pharmacovigilance practices	07-Nov-2018	European Medicines Agency
3	Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues	01-Dec-14	European Medicines Agency
4	Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: quality issues (revision 1)	01-Dec-14	European Medicines Agency
5	Biosimilar medicines: Overview	27-Sep-12	European Medicines Agency
6	Biosimilars in the EU: Information guide for healthcare professionals	27-April-17	European Medicines Agency
7	What I need to know about biosimilar medicines - information for patients	29 – Nov - 17	European Commission
8	Consensus information on biosimilars (23 languages)	29-Nov-17	European Commission
9	NICE Biosimilars Position Statement	06-Jan-15	National Institute for Health and Care Excellence
10	Commissioning framework for biological medicines (including biosimilars)	12-Sep-17	NHS England
11	Adalimumab best value biological medicines toolkit	July-18	NHS Commissioning Support Units

5.2.2 Additional information

#	Document Name	Publication Date	Publication Organisation
1	EMA scientific guidelines: multidisciplinary biosimilar	18 May 2015 (accessed date)	European Medicines Agency
2	EMA list of biosimilar medicines	Regularly updated	European Medicines Agency
3	Drug safety update: reporting suspected adverse drug reactions to vaccines and biological medicines Drug Safety Update - GOV.UK	22-Nov-12	Medicine and Healthcare products Regulatory Agency
4	Drug Safety Update: Biosimilar Products	01-Feb-08	Medicine and Healthcare products Regulatory Agency
5	Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes	2015	National Institute for Health and Care Excellence
6	Biosimilar medicines – NICE's approach	03-July-15	National Institute for Health and Care Excellence
7	Biosimilar medicines: a national prescribing framework	9-March-18	Healthcare Improvement Scotland
8	Biosimilar medicines: Key Therapeutic Topics	Updated Feb 18	NICE
9	Biosimilars adoption: resources	October 2017	The Cancer Vanguard
10	Biosimilars position paper	Revised December 2017	NRAS
11	Biosimilars for lymphoma	April 2017	Lymphoma Association
12	Trastuzumab biosimilars	June 2018	Breast Cancer Now
13	Diabetes UK position on the use of biosimilar insulin	July 2018	Diabetes UK
14	Switch management between similar biological medicines	July 2018	European Specialist Nurses Organisations
15	Biologic drugs in IBD	June 2018	Crohn's and Colitis UK
16	Is it safe to switch to a biosimilar?	Aug 2017	Specialist Pharmacy Service
17	Implementation of biosimilar MABs in Oncology	05-Feb-17	BOPA

5.2.3 Contact details for Patient Organisations

Organisation	Telephone	Email
Crohn's & Colitis UK	0300 222 5700	info@crohnsandcolitis.org.uk
Diabetes UK	0345 123 2399	helpline@diabetes.org.uk
Lymphoma Association	01296 619400	enquiries@lymphoma-action.org.uk
NRAS	0845 458 3969	enquiries@nras.org.uk

5.3 References and footnotes

- ¹ [Commissioning Framework for biological medicines \(including biosimilars\)](#), 2017
- ² [Commissioning Framework for biological medicines \(including biosimilars\)](#), 2017
- ³ European Medicines Agency: [Biosimilars in the EU; Information guide for healthcare professionals](#), 2017
- ⁴ *ibid*
- ⁵ Commissioning Framework for biological medicines (including biosimilars), 2017
- ⁶ Blood Journal: [Biosimilars: what clinicians should know](#), 2012
- ⁷ European Medicines Agency: [Biosimilar medicines: Overview](#)
- ⁸ European Medicines Agency: [Guideline on similar biological medicinal products](#), 2014
- ⁹ European Medicines Agency: [Biosimilars in the EU; Information guide for healthcare professionals](#) 2017
- ¹⁰ *Ibid*
- ¹¹ *Ibid*
- ¹² European Medicines Agency: [Biosimilar medicines: Overview](#)
- ¹³ **Note:** Although this is correct, not all biosimilars are made by recombinant technology and thus centrally regulated; low molecular weight heparins can be approved through decentralised or mutual recognition procedures, in selected countries.
- ¹⁴ European Commission: [Medicinal products](#)
- ¹⁵ European Medicines Agency: [Guideline on similar biological medicinal products](#), 2014
- ¹⁶ *Ibid.*
- ¹⁷ European Medicines Agency: [Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: quality issues](#) (revision 1), 2014
- ¹⁸ European Medicines Agency: [Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues](#), 2014
- ¹⁹ European Medicines Agency: [Product-specific biosimilar guidelines](#)
- ²⁰ European Medicines Agency: [Biosimilar medicines: Overview](#)
- ²¹ Blood Journal: [Biosimilars: the science of extrapolation](#). 2014
- ²² ICH Expert Working Group: [ICH harmonised tripartite guideline: Comparability of biotechnological/biological products subject to changes in their manufacturing process](#). 2004
- ²³ As of November 2018. Please refer to the [European Medicine Agency's website](#) for the latest list of biosimilars authorised in Europe, as there are many other biosimilar products in development. See also reference 13 (above).
- ²⁴ National Institute for Health and Care Excellence: NICE's biosimilars position statement, 2015
- ²⁵ *ibid.*
- ²⁶ Evidence summaries available from www.nice.org.uk/about/what-we-do/our-programmes/nice-advice/evidence-summaries
- ²⁷ *Ibid.*
- ²⁸ Future Focused Finance
- ²⁹ European Medicines Agency: [Biosimilar medicines: Overview](#)
- ³⁰ [MHRA biosimilar products](#), 2008
- ³¹ European Union: [EU directive \(2012/52/EU\)](#), 2012
- ³² European Medicines Agency: [Biosimilars in the EU; Information guide for healthcare professionals](#), 2017
- ³³ Healthcare Improvement Scotland, Biosimilar Medicines: A National Prescribing Framework, Revised March 2018
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- ³⁴ Medicines for Europe: [Biosimilars - Overview of positions on physician-led switching](#), 2018
- ³⁵ MHRA: [Yellow Card Scheme](#) 2018
- ³⁶ European Commission: [Medicinal products for human use, 2018](#)
- ³⁷ MHRA: [Yellow Card Scheme](#). 2018
- ³⁸ Medicines Healthcare Products Regulatory Agency: [Reporting suspected adverse drug reactions](#) to vaccines and biological medicines, 2012
- ³⁹ BioIndustry Association: Pharmacovigilance Specific Considerations for Biological Medicinal Products and Biosimilar Medicinal Products, 2012
- ⁴⁰ European Union: [Directive 2010/84/EU](#), 2010

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- ⁴¹ [EMA patient registries](#)
- ⁴² European Medicines Agency: [Biosimilar medicines: Overview](#)
- ⁴³ [Optimising medicines use, value and funding](#), December 2017
- ⁴⁴ European Medicines Agency: [Biosimilar medicines: Overview](#)
- ⁴⁵ Ibid
- ⁴⁶ [European Medicines Agency: Biosimilars in the EU; Information guide for healthcare professionals](#), 2017
- ⁴⁷ Ibid
- ⁴⁸ Ibid.
- ⁴⁹ Ibid
- ⁵⁰ European Medicines Agency: [Biosimilar medicines: Overview](#)
- ⁵¹ European Medicines Agency: [Biosimilars in the EU; Information guide for healthcare professionals](#), 2017
- ⁵² Ibid
- ⁵³ Coulter A, Collins A (2011). Making shared decision-making a reality: no decision about me without me. London, Kings Fund
- ⁵⁴ European Medicines Agency: [Summary of product characteristics](#)