

Biosimilar medicines

Key therapeutic topic

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[nice.org.uk/guidance/ktt15](https://www.nice.org.uk/guidance/ktt15)

Options for local implementation

- Biosimilar medicines have the potential to offer the NHS considerable cost savings and widen the access to innovative medicines.
- Develop and agree local policies to be aware when biosimilar medicines are coming to market and then support their managed introduction into care pathways safely and effectively, taking into account relevant regulatory advice, national guidance, patient factors and cost.
- Review and, if appropriate, optimise prescribing of medicines for which biosimilar medicines exist to ensure it is in line with these policies.
- Ensure all biological medicines, including biosimilar medicines, are prescribed by brand name so that products cannot be automatically substituted at the point of dispensing. The choice of whether a patient receives a biosimilar or originator biological medicine rests with the responsible clinician in consultation with the patient.

Evidence context

The NHS England publication, [What is a biosimilar medicine?](#) states that a biosimilar medicine is a biological medicine which is highly similar to another biological medicine already licensed for use. It is a biological medicine which has been shown not to have any clinically meaningful differences from the originator biological medicine in terms of quality, safety and efficacy. The continuing development of biological medicines, including biosimilar medicines, creates increased choice for patients and clinicians, increased commercial competition and enhanced value propositions for

individual medicines. Biosimilar medicines have the potential to offer the NHS considerable cost savings and widen the access to innovative medicines.

NICE position statement on evaluating biosimilars

NICE's position statement on [evaluating biosimilar medicines](#) was published in January 2015. This states that biosimilars notified to the NICE topic selection process for referral to the Technology Appraisal programme will usually be considered in the context of a Multiple Technology Appraisal, in parallel with their reference products in the indication under consideration. The Department of Health 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. In other circumstances, where it is considered a review of the evidence for a biosimilar medicine is necessary, NICE will consider producing an [evidence summary: new medicine](#).

Licensing and comparability

Biosimilar medicines introduced into the UK market are authorised by the [European Medicines Agency](#) (EMA). The EMA has produced a document covering a series of [questions and answers on biosimilar medicines](#). Biological medicines such as monoclonal antibodies, growth hormone and insulin are produced in or derived from living systems. The size and complexity of biological medicines, as well as the way they are produced, may result in a degree of natural variability in molecules of the same active substance, particularly in different batches of the medicine. The active substance of a biosimilar and its reference medicine is essentially the same biological substance but, just like the reference medicine, the biosimilar has a degree of natural variability. When approved, this variability and any differences between the biosimilar and its reference medicine will have been shown not to affect safety or effectiveness.

In the development of a biosimilar, there is no requirement to demonstrate clinical benefit to patients per se as this has been shown for the reference medicine. Instead, biosimilars undergo a comprehensive regulatory process which demands extensive comparability studies that demonstrate similarity to the reference medicine. The benefits and risks are then inferred from the similarity of the biosimilar medicine to the reference medicine in terms of quality, efficacy and safety. Biosimilar medicines are usually licensed for all the indications in the licence of the originator biological medicine, but this requires appropriate scientific justification on the basis of demonstrated or extrapolated equivalence. They are generally used at the same dose and route of administration as the biological reference medicine and have the same contraindications and

warnings in their summaries of product characteristics. However, the ongoing safety of any biosimilar or originator biological medicine is monitored separately (see below).

Any biological drug is likely to be modified several times during its production history and development, for example when there is a change in manufacturing process. After each such change, a similar comparability exercise that is carried out for a biosimilar is carried out to ensure that the new biological drug is similar to the old one. Therefore from a scientific and regulatory point of view, the active substance of the biosimilar could be viewed as just another version of the active substance of the originator. See the NHS publication [Answers to commonly asked questions about biosimilar versions of infliximab](#) and the NHS England publication, [What is a biosimilar medicine?](#) for more details.

Brand name prescribing and pharmacovigilance

In the UK, the MHRA recommends that all biological medicines, including biosimilar medicines, are prescribed by brand name ([February 2008 edition of Drug Safety Update](#)). Because biosimilar and reference biological medicines that have the same international non-proprietary name (INN) are not presumed to be identical in the same way as generic non-biological medicines, brand name prescribing ensures that the intended product is received by the patient. It ensures that products cannot be automatically substituted at the point of dispensing. The choice of whether a patient receives a biosimilar or originator biological medicine rests with the responsible clinician in consultation with the patient.

Pharmacovigilance is important for biosimilar medicines and every biosimilar authorised by the EMA will have a risk management plan in place (details of which will be in the European Public Assessment Report). Based on similarity being demonstrated with the reference medicine, the biosimilar can also refer to the safety experience gained with the reference medicine. As with all new medicines, biosimilars have a 'black triangle' in the first years after approval and any suspected adverse drug reactions should be reported through the Yellow Card Scheme (see the [June 2009 edition of Drug Safety Update](#) on the black triangle scheme for more information).

Patient registers are used to monitor for emerging safety and efficacy issues with biological medicines, and the MHRA supports the recording of brand names and batch numbers for traceability when reporting suspected adverse drug reactions ([November 2012 edition of Drug Safety Update](#)). The NHS Specialist Pharmacy Service has developed a validated tool to determine potential safety issues associated with new medicines, and these 'in-use product safety assessment reports' will be published for new biosimilar medicines as they become available. The in-use product safety assessment reports for the infliximab biosimilars, [Inflectra](#) and [Remsima](#) and the

etanercept biosimilar, [Benepali](#) state that brand name prescribing is vital if products are to be identified appropriately at the points of dispensing and administration. As with all biological medicines, for each patient, a traceable record of the brand, batch number, and presentation of the product used should be made. Reporting and monitoring of patients through clinical registries will enable collection of specific data on serious adverse events, and these mechanisms will act in addition to routine pharmacovigilance activities. Safe introduction and ongoing safe use of biosimilars requires practitioner, patient and manufacturer engagement with these processes.

Managing the introduction of biosimilar medicines

NHS England are undertaking a [programme of work](#) to improve clinician confidence and clarify understanding amongst decision makers, such as commissioners, clinicians, pharmacists and patients in their consideration of the appropriate use of biosimilar medicines. This includes the publication of [What is a biosimilar medicine?](#) and a collaborative work programme to improve education and understanding of both the theory and practical considerations related to biosimilar medicines. NHS England are working with NHS Clinical Commissioners, regional Medical Directors and Academic Health Science Networks to maximise the opportunities of a more competitive biological medicines market for the benefit of patients.

The NICE adoption resource [introducing biosimilar versions of infliximab: Inflectra and Remsima](#), was produced to help manage the introduction of biosimilar medicines into care pathways safely and effectively. NHS organisations shared their learning and experiences of introducing biosimilar medicines and these are presented as a series of examples of current practice. They are not presented as best practice but as real-life examples of how NHS sites have planned and managed the introduction of biosimilars. Local organisations will need to assess the applicability of the learning from the examples of current practice, taking into consideration the time, resources and costs of an implementation programme.

The NHS staff involved in the production of the NICE adoption resource reported that the use of biosimilars can reduce costs, allowing more treatment with new medicines, as long as the appropriate follow-up and monitoring systems are in place to manage risk and patient needs and expectations. Particular tips for managing the introduction of biosimilar medicines included:

- Identify clinical and pharmacy champions to take the lead in introducing biosimilars.
- Consult all stakeholders (including patients) to ensure confidence in using biosimilars.

- Provide information about the EMA licensing process for biosimilars, extrapolation and equivalence, and the manufacturing process (including intra-product manufacturing changes for both biological medicines and their biosimilars).
- Identify the potential cost-saving and re-investment opportunities and explore gain-share agreements.
- Seek formal approval at the local formulary committee once there is clinical consensus to include biosimilars on the formulary.
- Collect baseline data and agree metrics to be collected during and after the introduction of biosimilars.
- Submit data to national audits and registries.

In February 2016, the British Society of Gastroenterology published [guidance on the use of biosimilar infliximab \(Inflixtra and Remsima\) in inflammatory bowel disease](#). This recommends that there is sufficient evidence to recommend that patients who are in a stable clinical response or remission on Remicade therapy can be switched to Remsima or Inflectra at the same dose and dose interval. This should be done after discussion with individual patients, with explanation of the reason for switching (which is usually on the grounds of benefit to the overall service by reduction in costs of the drug and its administration).

An evidence summary: new medicine publication on the [insulin glargine biosimilar \(Abasaglar\)](#) is also available.

Prescribing data

Biosimilar versions of epoetin, filgrastim and somatropin have been available for some time. As for all medicines, the safety of biosimilar medicines is continuously monitored after authorisation, and no particular safety concerns have arisen for these biosimilar medicines that have required regulatory action to be taken. Recently, biosimilar versions of infliximab ([Inflixtra](#), [Remsima](#) and [Flixabi](#)) etanercept ([Benepali](#)) and insulin glargine ([Abasaglar](#)) have been launched in the UK. Further biosimilar versions of adalimumab, bevacizumab, pegfilgrastim, rituximab and trastuzumab are expected to be available in the next few years.

Biosimilars have the potential to offer the NHS considerable cost savings, especially as biological medicines are often expensive and are often used to treat long-term conditions. The NHS England publication, [What is a biosimilar medicine?](#) states that biosimilar medicines are more challenging and expensive to develop than generic medicines. Whilst they cannot offer the same percentage

price reductions as traditional generic medicines, nevertheless, there are significant savings associated with increased competition between biological medicines, including biosimilar medicines. Recent research has given clear evidence that the additional competition is bringing value and opportunity to widen access for patients in some circumstances. However, this research also demonstrates that biosimilar medicine uptake across Europe to date shows very different patterns, depending on the class of biological medicine and the procurement measures in place. Costs for both biosimilar and originator biological medicines may vary locally depending on local contractual arrangements, and Regional Pharmacy Procurement Specialists will be able to provide more details.

There are currently no medicines optimisation key therapeutic topic (MO KTT) prescribing comparators for this topic. The development of prescribing comparators to support this key therapeutic topic is currently being explored by the NHS England Medicines Optimisation Intelligence Group^[1].

The [Medicines optimisation dashboard](#), which brings together a range of medicines-related metrics from across sectors, includes a prescribing metric on biosimilars. This is the proportional split of the use of the originator biological medicine and biosimilar versions of infliximab by volume. There is an intention to include other biosimilar medicines in the medicines optimisation dashboard as they become available. The medicines optimisation dashboard helps NHS organisations to understand how well their local populations are being supported to optimise medicines use and inform local planning. The dashboard allows NHS organisations to highlight variation in local practice and provoke discussion on the appropriateness of local care. It is not intended as a performance measurement tool and there are no targets.

There is also a prescribing metric on biosimilars in the [NHS Improvement Model Hospital portal](#) [requires log in]. This is the percentage total etanercept/infliximab usage (by month) that is for the biosimilar product not the originator product. The data are provided using the Define benchmarking tool which 85% of acute trusts in England have purchased licences for and provide data into. The metric uses the defined daily dosage (DDD) of the biosimilar product used in a month as the numerator and the total DDD of the originator and biosimilar product used as the denominator. The data are displayed as a time series to show improvement over time and usage against other trusts and the national median. Since launch, the uptake of biosimilar infliximab and etanercept has been variable across the country, with early adopter sites rapidly achieving greater than 90% adoption whilst other sites have limited or no uptake. The model hospital is being developed to support the principles and objectives developed from the Carter Review, [Operational productivity and performance in English NHS acute hospitals: unwarranted variations](#). In addition to a range of infrastructure and service delivery related metrics, a range of clinical and medicines-

related metrics have been developed, with additional metrics being added. These are linked to national commissioning and medicines optimisation developments.

^[1] For details of any update to the comparators refer to the [NHS Digital](#) website and the [Information Services Portal](#), Business Services Authority.

Update information

January 2017: This topic was retained for the 2017 update of medicines optimisation: key therapeutic topics. The evidence context has been updated in the light of new guidance and important new evidence.

About this key therapeutic topic

This document summarises the evidence base on this key therapeutic topic which has been identified to support medicines optimisation. **It is not formal NICE guidance.**

For information about the process used to develop the Key therapeutic topics, see the [integrated process statement](#).

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