Position Statement on Biosimilars

Aneurin Bevan University Health Board endorses the appropriate use of biosimilars which will release cost efficiencies to support the treatment of an increasing number of patients and the uptake of new and innovative medicines. It is therefore expected that directorates will plan for the managed entry of new biosimilar medicines and consider how this will apply to both new and existing patients.

It is recognised that the evidence regarding interchangeability is still developing. Guidance 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.

Background

A biosimilar medicine is a medicine that is developed to be similar to an existing biological medicine. They differ from generic drugs which have simpler chemical structures and are considered to be identical to their reference medicines. The characteristics of biologic drugs cannot be reproduced exactly. To gain approval for use, biosimilar medicines have to demonstrate that they are as safe and as effective as the original reference medicine, and have the same quality.

Over the past 10 years there has been a rapid worldwide increase in the number of biological medicines that have received regulatory approval. Biosimilar medicines are developed in anticipation of an impending patent expiry of innovator biologic drugs.

A number of top-selling biological medicines have lost, or will be losing patent protection over the next few years, especially monoclonal antibodies that are tumour necrosis factor (TNF) inhibitors or receptor antagonists for use in patients with cancer, rheumatoid arthritis and other inflammatory disease, and insulins for diabetes.

Although biosimilars are already used to some extent in the NHS, and NICE has previously included biosimilars in its technology appraisal on the human growth hormone (somatropin), it is likely that their availability and use will become more widespread over the next few years. Biosimilars have the potential to offer the NHS considerable cost savings, especially as they are often used to treat long-term conditions.

Licensing of Biosimilars

The standard approach to licensing of a generic medicine, where the medicine must demonstrate bioequivalence (that is the bioavailability of the generic medicine must not differ significantly when given at the same dosage under similar conditions), is not sufficient for biosimilar medicines. For licensing in the European Union, the manufacturer of the biosimilar medicine must demonstrate that the medicine is:
i) Similar to the original reference product, and
ii) Do not have any meaningful differences from the original reference product in terms of quality, safety or efficacy.

However, if biosimilarity has been demonstrated for one indication or clinical situation, the licence may be extrapolated to a broader range of indications if appropriate scientific justification is provided.

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 can then be inferred from the similarity of the biosimilar product to the reference product in terms of quality, efficacy and safety.

Biological medicines, including biosimilars, are derived from living organisms and produced using complex manufacturing processes. This results in variability from batch to batch. This difference is not seen in the manufacturing of chemical medicines. 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. In the case of Remicade, the infliximab reference medicine, there have been 40 listed changes made to the manufacturing process for the active substance or the final product since its original authorisation (1999–2011). After each such change, the same 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.

Prescribing and Pharmacovigilance

The evidence base for the safety and efficacy of biosimilar medicines has been established through the medicines regulatory process. However, there is limited experience, as yet, of the long term use and ease of interchangeability of biological medicines in clinical practice. Clinical experience and prescriber and patient confidence with biosimilar medicines is, therefore, still emerging. Switching to a biosimilar medicine should be managed at the discretion of the individual prescribing clinician.

It is recognised that some clinical specialties (for example rheumatology and dermatology) have more experience using and switching between a range of biological medicines than others (for example gastroenterology). Some clinical specialties may, therefore, be more comfortable switching to a biosimilar medicine, particularly where there is already experience of switching between different biological medicines. Emerging evidence on switching a biological medicine to a biosimilar medicine will continue to guide decisions on interchangeability in the future.

There are no specific efficacy or safety concerns identified for biosimilar medicines but, as for all biological medicines, clinical experience with biosimilar medicines is still emerging to guide their use. As for all new medicines, adverse drug reactions to biosimilar medicines should be reported through the Yellow Card Scheme.
Clinical outcomes for individual patients on any biological medicine should be measured using established recognised systems for monitoring disease activity and response to treatment. Clinical registries are being established for a number of biological medicines. It would be appropriate to explore the expansion of these databases to capture details of biosimilar medicines.

Biological medicines, including biosimilar medicines, should be prescribed by brand name and the brand name and batch number should be recorded on the patient’s prescription, case record or other appropriate clinical system.

The manufacturer’s patient information leaflet should be supplied to all patients receiving any medicine, including a biosimilar medicine.

In the UK, the MHRA recommends that all biological medicines, including biosimilar medicines, are prescribed by brand name (Drug Safety Update 2008).

As with all new medicines, biosimilars have a 'black triangle' in the first years after approval to make providers aware of the importance of pharmacovigilance (Drug Safety Update 2009). 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 (Drug Safety Update 2012).

Local Implementation

**NICE / AWMSG position 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.

AWMSG will no longer routinely appraise all biosimilar medicines. Where the reference product has been recommended for use by AWMSG for the same indication(s) and in the same population, or was initially available prior to 1st October 2002, and the cost of the new biosimilar medicine is equivalent or lower that the reference medicine, the application will be routinely excluded from appraisal by AWMSG. A full submission will be required for indication(s)/populations where the reference product has been appraised by AWMSG/NICE and is not recommended for use, or in circumstances where the reference medicine has been licensed post October 2002 but has not been appraised by AWMSG/NICE.

**Tips from the NHS for managing the introduction of biosimilar medicines**

- 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
  ✓ the manufacturing process and 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
• Project management

According to NICE Adoption and Impact Programme that in order to gain maximum benefit, biosimilar medicines should be adopted using a project management approach.

Project team

The first step in this approach is to form a local project team who will work together to introduce biosimilar medicines and manage any changes in practice.

Individual NHS organisations will determine the membership of this team and how long the project will last. In order to introduce biosimilars in an effective and sustainable way, consider the following membership of the team:

• Clinical champion(s): a consultant clinician/physician in the relevant field.
• Pharmacy lead: this could be a specialist procurement pharmacist or a medicines management pharmacist
• Management sponsor: will be able to help assess the financial viability of the project, drive the formulation of a business case and help to demonstrate the cost savings achieved and will have responsibility for negotiating any gain-share agreements.
• Other stakeholders or staff: these may include nursing and other ward staff who will be valuable members of the project team as they will be involved in providing the service.

Communication and collaborative working

The specific communications may include information on the following:

• Background to the proposed switch from a biological medicine to a biosimilar medicine including which patients may and may not be eligible.
• The timetable for the proposed switch, including detailed steps.
• Details of risk assessment and control measures put in place to mitigate risks during the switch-over phase.
• The requirements and arrangements for clinical audit
• Who to contact for further information and how to report problems.
• clear written and verbal communication may include:
• Letters to hospital consultants, departments, general practice and patients.
• Dissemination of information at directorate, departmental and team meetings.
Resource impact

Biosimilar medicines have the potential to offer the NHS considerable cost savings, especially as they are often used to treat long-term conditions. NICE has published a costing statement, implementing the NICE guidance on biosimilar versions of infliximab. The statement highlights that, in the context of this guidance, using biosimilar infliximab may lead to drug cost savings for Health Board. The statement shows a cost saving of 10% per cycle by changing to a biosimilar version of infliximab. However, costs may vary locally depending on local contractual arrangements and it is reported that some centres have achieved much greater cost savings.

The implementation team should treat the development of a robust business case as an early priority in the life of the implementation project.

Dr Syed M Ayas  
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Further reading:


British Society of Gastroenterology. 2015. *IBD Section Statement on Biosimilar drugs*

European Commission. 2013. *What you need to know about biosimilar medicinal products. Process on corporate responsibility in the field of pharmaceuticals access to medicines in Europe: a consensus information document*

European Medicines Agency. 2012. *Questions and answers on biosimilar medicines (similar biological medicinal products)*


London and South East Regional Medicines Information Service. 2015. *Answers to commonly asked questions about biosimilar versions of infliximab*


PrescQIPP. 2015. *Webinars on biosimilars (secondary care and primary care)*


UK Medicines Information. 2015. *In-use product safety assessment report: Remsima and Inflectra (infliximab biosimilars)*


*What are biosimilars and are they important?* 2013. *Drug and Therapeutics Bulletin.* 51:57-60