Biosimilar medicines position statement and guidance

(This document is a locally abridged and adapted version of the NHS England publication, 'What is a Biosimilar Medicine?'[1].)

Basingstoke, Southampton & Winchester District Prescribing Committee (DPC), supports the appropriate use of biosimilars which will drive greater competition to release cost efficiencies to support the treatment of an increasing number of patients and the uptake of new and innovative medicines.

1. Executive summary

1.1. Biological medicines are medicines that are made or derived from a biological source and as such are complex, with inherent variability in their structure.

1.2. 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.

1.3. Biosimilar medicines are not considered generic equivalents to their originator biological medicine because the two products are similar but not identical. However, they will have met regulatory requirements in terms of comparative quality, safety and efficacy.

1.4. Where NICE has already recommended the originator biological medicine, the same guidance will normally apply to a biosimilar of the originator.

1.5. Where the originator biological medicine is on the local medicines formulary, biosimilars of the originator will also be included on the formulary following approval by commissioners and providers. The available products will be identified by brand name.

1.6. In line with MHRA guidelines, biological medicines, including biosimilar medicines must be prescribed by brand name to support on-going pharmacovigilance of the individual products.

1.7. The decision to prescribe a biological medicine for an individual patient, whether an originator or biosimilar medicine, rests with the responsible clinician in consultation with the patient.

1.8. At the time of dispensing, a biosimilar medicine will not be automatically substituted for the originator or other biosimilar by the pharmacist.

1.9. Switching patients from one biological medicine to another biological or biosimilar medicine should be a multidisciplinary approach involving the clinician, patient, specialist nurse and pharmacist, and should include plans for managing education, communication, procurement, administration and monitoring.

1.10. 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.

1.11. Discussions should take place between commissioners and providers as to how savings released from the use of biosimilar medicines will be appropriately

shared, to allow re-investment in the individual services affected and/or other patient services across the NHS.

2. Background

2.1. Biological medicines have revolutionised patient treatment by offering new and effective medicines for acute and chronic conditions. As the patent expires for individual originator medicines, biosimilar medicines can be introduced to provide additional options for patients and the NHS. There is an increasing range of biosimilar medicines available and in development.

2.2. Making the most of biosimilars in our healthcare systems requires investment in education, experience and use, establishing sustainable and appropriate procurement, and transparent and clear decision-making frameworks.

3. What is a biosimilar medicine?

3.1. 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.

3.2. A biosimilar medicine is a biological medicine that is developed to be highly similar and clinically equivalent to an existing biological medicine. A biosimilar contains a version of an active substance of an already approved biological medicine, which is referred to as the ‘reference medicine’ or ‘originator medicine’. Similarity to the reference medicine in terms of quality, structural characteristics, biological activity, safety and efficacy must be established based on a comprehensive scientific comparability exercise such that they do not have any clinically meaningful differences from the reference medicine in terms of quality, safety and efficacy.

3.3. 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.

4. How are biosimilar medicines authorised for use?

4.1. Marketing authorisation applications for biotechnology-derived medicines, including biosimilar medicines, are by law reviewed centrally by the European Medicines Agency (EMA). Biosimilar medicines require distinct regulatory pathways from those applied to generic medicines as they are not exact replicates of the originator (reference) medicine. The shortened and simplified regulatory approval process used for generic medicines is not sufficient to demonstrate similarity.

4.2. In 2003, the EU adopted a specific regulatory pathway that provides a robust regulatory process 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. 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.

4.3. All biologics 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 by the regulator to ensure that any changes do not impact the quality, safety and efficacy of biological medicines. The scientific basis for this regulatory pathway is the same as that used for manufacturing changes.

4.4. Depending on the evidence provided for regulatory assessment of the biosimilar medicine, it will typically have all of the therapeutic indications established by the reference medicine. Although there may not be comparative clinical data (phase III studies) in all of these indications for the biosimilar, the data package submitted when considered in totality will 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.

5. NICE position[2]

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

5.2. NICE can decide to apply existing guidance, to relevant licensed biosimilar products which subsequently appear on the market. Therefore, where NICE has already recommended the reference medicine, that same guidance is likely to apply to the biosimilar medicine.

5.3. 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 summary: new medicine' (ESNM). ESNMs will use the brand names of the medicines because substitutability and interchangeability cannot be assumed. ESNMs are not formal NICE guidance and so do not make recommendations.

5.4. The decision regarding the choice of biosimilar or originator biological medicine for an individual patient rests with the responsible clinician in consultation with the patient.

5.5. 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.

6. Why should biosimilar medicines be used?

6.1. Competition between different biological medicines, including biosimilar medicines, creates increased choice for patients and clinicians, and enhanced value propositions for individual medicines. There are additional benefits, such as further sources of supply.

6.2. 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.

6.3. Recent research has given clear evidence that the additional competition is bringing value and opportunity to widen access for patients in some circumstances.

7. What considerations should inform decision-making over choice of product?

7.1. Those making decisions about whether to use a biosimilar product in place of the originator should consider the following questions in each case:

- Which patient groups will be included, e.g. particular indications, adults/paediatrics, new/existing patients?
- Is the biosimilar licensed for all the indications and routes of administration required?
- Is the biosimilar available in suitable strengths and presentations?
- Is the administration device acceptable to the patient and are product-associated support services available?
- Do homecare services need to be considered?
- How will patients be engaged with the decision and process?
- How will prescribers, nurses, pharmacists, patients and carers be educated and prepared?
- What additional patient monitoring will be required?
- What procurement arrangements are in place, e.g. regional purchasing frameworks?
- How secure is the supply chain?
- Are there any differences in storage condition requirements?
- How will prescribing and stock be safely separated from the originator and other biosimilar products?
- How will the savings be used to benefit patients in this and/or other services?

7.2. General considerations for biosimilar medicines

7.2.1. Biosimilar medicines are approved to be therapeutic equivalents to the reference medicine, establishing that the previously proven safety and efficacy of that medicine also applies to the biosimilar. As with any biological medicine, the biosimilar medicine will have details of its licensed indications included in the British National Formulary.

7.2.2. Treatment decisions should be made first on the basis of clinical judgement for individual patients and secondly on the basis of the overall value proposition offered by individual medicines.

7.2.3. The role of the physician in treating patients with these complex medicinal products is particularly important.

7.2.4. Patient consultation, which takes into account their needs, preferences and values, is also an essential part of evidence-based medicine. Clinicians should seek to use all available evidence to guide decisions about the care of the individual patient.

7.2.5. Care should be taken not to damage patient confidence and introduce risk by making multiple product changes in quick succession according to fluctuations in purchase price.

7.2.6. There is growing practical NHS experience that demonstrates the safety and efficacy of biosimilars in clinical practice.

7.2.7. It is recommended that switching between a reference product and its biosimilar (and indeed amongst biosimilar medicines) should be managed at the discretion of the prescriber in partnership with the patient and wider multidisciplinary team, with appropriate monitoring in place.

7.2.8. Evolving evidence and treatment guidance should be made available to patients and prescribers to support them in their decision-making.

7.2.9. Automatic substitution (the practice of dispensing one medicine instead of another equivalent and interchangeable medicine at the pharmacy level without consulting the prescriber) is not appropriate for biological medicines, including biosimilar medicines, and is not permitted.

7.2.10. As biosimilar medicines often use the same international non-proprietary name (INN) as their reference product, the main way to ensure automatic substitution does not take place is through brand name prescribing. Brand name prescribing must be adhered to by all prescribers for biological medicines, including biosimilar medicines.

7.2.11. Prescribing using the INN, or 'generic' name, is established practice within the NHS for most products. It is important to ensure that prescribers are aware of the different requirements associated with biological medicines, including biosimilar medicines.

8. Pharmacovigilance monitoring

8.1. EU pharmacovigilance legislation mandates that all biological medicines, including biosimilar medicines, approved after 1 January 2011, are subject to additional monitoring for safety. Medicines under additional monitoring have a black inverted triangle (▼) in their labelling. The triangle highlights it is a new product and encourages both prescribers and patients to report suspected adverse drug reactions (ADR) to the MHRA Yellow Card scheme.

8.2. The MHRA requests those reporting a suspected ADR to a biological medicine to provide the brand name and specific batch number on any ADR report. The MHRA also asks that the brand name and batch number is provided to patients and carers when the product is administered, to help them report an issue more accurately.

8.3. 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.

References:

1. NHS England, Medical Directorate. What is a Biosimilar Medicine? Guide. Biosimilarguide.pdf, accessed 27/4/16.
2. National Institute for Health and Care Excellence. NICE's Biosimilar Position Statement. Biosimilars statement.pdf, accessed 27/4/16.

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