Q&A 300.4

What are biosimilar medicinal products?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals
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Background

Medicinal products called biosimilars have been on the UK market since 2006 when Omnitrope® (somatropin, recombinant-DNA growth hormone) was licensed (1). These products are also referred to as "follow-on biologicals", "subsequent-entry biologicals" or "similar biotherapeutic products" (2).

Answer

Biosimilar medicines are described by the European Medicines Agency (EMA) as biological medicines that are developed to be similar to an existing biological medicine (the 'reference medicine'). An authorised biosimilar is generally used at the same dose to treat the same conditions (3).

Biological medicines are derived from living cells or organisms and consist of large, highly complex molecular entities which may be difficult to characterize. Due to the variability of the biological system and the manufacturing process, biological medicines show a certain degree of variation, even between batches of the same product. As a result of differences in the manufacturing processes, biosimilars will not be completely identical to the 'reference medicine' (4).

Since the patents for several biological medicines have either expired, or are due to expire, a number of biosimilars have been licensed and more are currently being developed (4). However, the majority of the original biological medicines manufacturer's product information is proprietary, and details of the manufacturing process may not be disclosed, even after patent expiry of the product (2).

A regulatory framework is in place in the European Union for authorising biosimilars. Comparability studies are required to show the similar nature, in terms of efficacy, safety and quality, of a new biosimilar product with the chosen reference medicinal product that has already been authorised for use in Europe. This is different to the standard generic approach for a conventional medicinal product in which a company has to simply demonstrate bioequivalence with a reference product by appropriate bioavailability studies (5). Product-specific biosimilar guidelines have also been issued by the EMA (6).

The Association of the British Pharmaceutical Industry (ABPI) has issued a position paper on biosimilar medicines, which makes seven recommendations for regulators, Health Technology Assessment (HTA) agencies, NHS Commissioners and healthcare professionals (7). A briefing paper on biosimilar medicines has also been published by the British Generic Manufacturers Association (8). The National Institute for Health and Care Excellence (NICE) has also recently updated its methods for providing guidance and advice on biosimilars (9). A national prescribing framework for biosimilars has been published by Health Improvement Scotland to inform clinical decision-making and support the safe, effective and consistent use of biosimilar medicines in NHS Scotland (10). Similarly, NHS England has recently published a document entitled "What is a biosimilar medicine?" which aims to "provide an update for key clinical and non-clinical stakeholders about the developing 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" (11).

Biosimilars are not generic medicinal products and products (biosimilar and reference) that have the same international non-proprietary name (INN) are not presumed to be identical (12). Therefore, when prescribing biological products, brand name prescribing should be adhered to, in line with recommendations from the Medicines and Healthcare products Regulatory Agency (MHRA) and NICE, as well as being enshrined in EU Law (11). Brand name prescribing ensures that automatic substitution of a biosimilar product does not occur when the medicine is dispensed (12). Similarly, the brand name and batch number of the specific medicinal product given to the patient should be clearly identified when reporting "yellow card" events (e.g. use the brand names *Binocrit* or *Eprex*, rather than epoetin alfa) (12,13).

A review has highlighted that using biosimilars may reduce costs and increase access to biological treatments (4). However, biosimilars cannot be thought of in the same way as traditional generic drugs. Whilst the efficacy, safety and quality of biosimilars are evaluated during the licensing process (4,14), those making decisions about whether to purchase a biosimilar should consider the following questions:

- How might any differences from the originator product, for example safety, be monitored? (4).
- Is the biosimilar available in suitable strengths and presentations?
- Is the biosimilar licensed for all the indications and routes of administration required? [The European Medicines Agency has issued guidelines on the extrapolation of efficacy and safety data from one therapeutic indication to another (14)].
- Is the administration device acceptable to the patient and are product-associated support services available? (15).

Examples of biosimilar products that have reached the UK market* (16,17)

Reference product	Biosimilar product
Genotropin® (somatropin)	Omnitrope®
Eprex® (epoetin alfa)	Binocrit® (epoetin alfa) Retacrit® (epoetin zeta)
Neupogen® (filgrastim)	Accofil®▼ Nivestim® Ratiograstim®▼ Zarzio®
Remicade® (infliximab)	Inflectra®▼ Remsima®▼
Gonal-f® (follitropin alfa)	Bemfola®▼

*this list is not exhaustive

Summary

- Biosimilar medicines are described by the European Medicines Agency (EMA) as biological medicines that are developed to be similar to an existing biological medicine (the 'reference medicine') (3).
- Biological medicines are derived from living cells or organisms and consist of large, highly complex molecular entities which may be difficult to characterize (4). As a result of differences in the manufacturing processes, biosimilars cannot be presumed to be identical to the 'reference medicine' (4,12).

- A regulatory framework is in place in the European Union for authorising biosimilars. Comparability studies are required to show the similar nature, in terms of efficacy, safety and quality, of a new biosimilar product with the chosen reference medicinal product that has already been authorised for use in Europe (5).
- Biosimilars are not generic medicinal products and products (biosimilar and reference) that have the same international non-proprietary name (INN) are not presumed to be identical (12). Therefore, when prescribing biological products, brand name prescribing should be adhered to, to ensure that automatic substitution of a biosimilar product does not occur when the medicine is dispensed (11,12). It is also essential to identify the brand name when reporting adverse drug reactions (12,13).

Limitations

- This Medicines Q&A provides a general overview of the published information available about biosimilar medicinal products. Examples of publications produced by various national bodies are included in this Medicines Q&A and should be referred to for more detailed information on this topic (8-11).
- Only examples of products that have been launched in the UK have been included in the table. Since the patents for several biological medicines have either expired, or are due to expire, a number of biosimilars have been licensed and more are currently being developed (4).
- Other biosimilar products may have been licensed in the EU but not yet launched in the UK.
- The clinical efficacy, safety and cost-effectiveness of biosimilar products have not been considered in this Medicines Q&A.

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Quality Assurance

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Search strategy
- Medline (via NICE Evidence Search): exp *BIOSIMILAR PHARMACEUTICALS/ (limited to human, English language and review articles)
- Embase (via NICE Evidence Search): “BIOSIMILAR” (1980-2011)
- Embase (via NICE Evidence Search): exp*BIOSIMILAR AGENT/ (limited to human, English language and review articles and 2011-2015)
- Electronic Medicines Compendium (eMC). Accessed via http://www.medicines.org.uk/emc/
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