Is it safe to switch to a biosimilar medicine?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals
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Date prepared: 31st August 2017

Background

Biological medicines are derived from living cells or organisms and consist of large, highly complex molecular entities (1,2). Biosimilar medicines, also referred to as “follow-on protein products”, “subsequent-entry biologicals” or “similar biotherapeutic products”, are described by the European Medicines Agency (EMA) as biological medicines that are developed to be highly similar to an existing biological medicine (the ‘reference medicine’ or ‘originator’) (3,4). Further background information on biosimilar medicines is available from (2,5-7):

- EMA (2017): Biosimilars in the EU: Information guide for healthcare professionals
- British Biosimilars Association website: Facts about Biosimilars; Resources; Hot Topics

Biological medicines are often expensive and are frequently used to treat long-term conditions (8). Since biosimilars are typically available at a reduced price to the reference medicine, their use has the potential to offer the NHS considerable cost savings and widen patient access to innovative treatments. In England, a number of organisations, including the National Institute for Health and Care Excellence (NICE) and NHS England have identified use of biosimilar medicines as a high priority topic for medicines optimisation. NHS England are now urging a more proactive and collaborative approach between commissioners, providers and patients to realise the potential savings from switching to biosimilar medicines (9).

With over 10 years clinical experience across the EU, confidence in the safety and efficacy of biosimilar medicines for their approved indications has grown, and this has alleviated some of the initial concerns about their use, particularly when initiating therapy in treatment-naïve patients (3,5). But is it safe to switch patients already established on a biological medicine to a biosimilar?

In this Q&A, the term switching will be used in the context of a single switch from the reference (originator) biological medicine to a biosimilar medicine. At present data on multiple switches, i.e. switching back and forth between the originator and a biosimilar, and on switching from one biosimilar to another, are limited (9-11).

Answer

When deciding whether or not to switch patients from an originator biological medicine to a biosimilar, it is important to explain the reasons for switching, and to respect and address concerns that patients and/or their clinician may have (8,12).

Reasons for switching

As no changes in clinical outcomes are expected, the reasons for switching are likely to be non-clinical, primarily for cost saving, and these should be fully and transparently discussed with patients to help them understand the wider benefits, while ensuring prices remain confidential within the NHS (9,13-16). Over the last ten years, the NHS has already benefitted from savings and is getting better at adopting biosimilars, but more needs to be done to avoid falling further behind many other European countries (7,9). A recent NHS England commissioning framework for biological medicines outlines aims to increase
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uptake of biosimilars to deliver savings of at least £200m to £300m per year by 2020/21, with at least 80% of existing patients to be prescribed the “best value biological medicine” within one year of launch of a biosimilar (9).

The cost savings generated by switching patients to biosimilars can facilitate more efficient allocation of limited NHS resources, potentially improving patient care, as well as increasing earlier access to biological treatments for more patients. Experience also suggests switching provides incentive for the originator pharmaceutical companies to reduce prices or make improvements to the originator, or to research and develop new medicines (7,9,17). In a small survey conducted by the National Rheumatoid Arthritis Society (NRAS), patients were asked “If your biologic was switched to a cheaper but equally good/safe drug to save money for NHS, what would be most important for you to know?”. 40.4% of patients stated they didn’t mind switching “so long as the treatment works as well as my existing treatment” and a further 27.3% hoped “that someone who couldn’t otherwise get onto biologic treatment would benefit.” (7).

However, it should be considered that keeping patients fully informed, and providing additional monitoring for patients switching to a biosimilar will come with administrative and time costs, and with the current NHS arrangements for funding high cost medicines, there is no direct incentive for providers (i.e. NHS Trusts) to undertake a switch programme (9,13,18). NHS England therefore supports commissioners to make use of appropriate financial incentives to cover these costs, although would expect these to cease once prescribing of the biosimilar was established (9).

Experience of successful switch programmes implemented in some NHS trusts has been reported (9,18). At the Mid Yorkshire Hospitals NHS Trust, pharmacy-led switching programmes for infliximab and etanercept resulted in around 85% of patients switching to a biosimilar (9). Patients were reported to have a good understanding of the benefits of saving money through biosimilars, notably to reinvest in wider services. The Trust’s Medicines Information Patient Helpline was utilised to facilitate patient education and engagement, and assuage concerns. At the University Hospital of Southampton NHS Trust, cost savings from switching gastroenterology patients to infliximab biosimilar enabled employment of a full-time specialist nurse, and updating of systems, to improve patient care, and collection and reporting of efficacy and safety data (9,18). Seeing some of the cost savings reinvested in improvements to their care was considered a major motivation for patients, and good communication with patients was considered by the clinical team as vital to successful implementation of the switch programme. In other hospitals and primary care settings, savings have contributed to provision of specialist pharmacists to oversee and aid the switch process, providing support for patients, and freeing up other clinical staff to focus on routine service delivery (9).

Addressing Concerns

Concerns about switching are most likely to be related to potential differences in quality, efficacy and safety of the biosimilar, and interchangeability with the reference product (19). A clear explanation of the science and regulatory processes required for EU authorisation possibly in the form of an information leaflet, may serve as reassurance that they can be considered as equivalent in quality, efficacy and safety to the reference product. This could highlight the considerable duration of clinical experience with a number of biosimilars (38 at the time of writing). (2,7,12,20,21).

The EU has led the way in the regulation and development of biosimilar medicines globally, providing a solid framework for their approval (3,22). The first biosimilar, Omnitrope® (somatropin, recombinant-DNA growth hormone), was licensed by the EMA in 2006 (23). EMA guidelines have been adopted or used to inform guidelines in numerous other countries, as well as by the World Health Organization (WHO) (5,24).
To receive a marketing authorisation from the EMA, a new biosimilar must provide data from well-designed, comprehensive **comparability studies**, including pharmacokinetic and pharmacodynamic studies, and from pivotal clinical trials to demonstrate high similarity to the reference medicine in terms of structure, biological activity and efficacy, safety and immunogenicity profile (3,4,25). This process is more detailed than the simpler process applied to generic medicines, and development of a biosimilar can take several years (23,26,27). But it is considered necessary as biosimilars are more complex than generics, and thus will not be completely identical to the reference medicine (6,26,28). Concerns about structural differences are greater for the larger, more complex biological medicines such as monoclonal antibodies, compared to smaller, less complex products such as insulins or low molecular weight heparins (29,30).

Consequently the type and extent of clinical data required to demonstrate biosimilarity will vary on a case by case basis, and the aim is to ensure that any differences will be minor and not “clinically meaningful” (3,6,28). Biosimilarity is considered demonstrated based on the “totality of evidence” from all the studies, with each step in the development program supporting the preceding one (27,31).

- **Quality**

There may be concern that biosimilars are ‘cheap copies’ of the reference medicine (21). This may apply in some countries where less strict regulatory guidelines allow for approval of agents that cannot be considered as biosimilars but may instead be referred to as “intended copies” or “biomimics” (32,33). But it is not the case in EU countries where, as with all medicines, the manufacturing of biosimilars is strictly regulated.

To meet EMA requirements, biosimilar manufacturers must hold a licence and will require sophisticated, state-of-the-art manufacturing technology (21,31). They will need to apply substantial knowledge, experience and expertise to extensively analyse the reference medicine and reverse engineer a highly similar agent, and demonstrate consistency and robustness of their manufacturing process through compliance with good manufacturing practices (GMP), modern quality control and assurance procedures, in-process controls and process validation (21,31,34). Manufacturing premises are subject to regular inspection, and the same strict requirements and inspections apply if any manufacturing steps take place outside the EU (21). Before batches of any biological medicines, including biosimilars, are released, they must meet the required standards for physicochemical properties, biological activity, purity, sterility and stability (5). The EMA requires that “the impurity profile and the nature of excipients of the biosimilar itself do not give rise to concern” (25). Clinicians and patients can thus be reassured that the reason biosimilars can be marketed at a lower price is not because they are lower quality, but because they benefit from a less cost-intensive development program (33).

Further information on the manufacturing processes for biological medicines is available as a factsheet from the Association of British Pharmaceutical Industries (ABPI) and British Biosimilars Association “Biological medicines: what you need to know about manufacturing?” (35).

- **Efficacy**

The regulatory process should provide assurance that a biosimilar will be as effective as the reference medicine; nonetheless patients and clinicians may remain concerned about a loss of efficacy when switching (5,12,21). Patients may therefore need reassurance that their condition will be appropriately monitored during the process (9,18). If concerns are related to the minor differences between the products, it may also be highlighted that, although the active substance remains the same, all biological medicines have a degree of natural variability (heterogeneity), particularly in different batches of the same medicine (known as batch-to-batch variability), and this applies equally to biosimilars and the reference medicine (2,3,6,8,18,35,36). Another key discussion point is that originator products can go through a number of variations post marketing, often resulting in improvements to the quality of the product, such that the reference product on the market today could be considered a biosimilar to the one...
that underwent clinical trials (2,12,18,26,37,38). For example, in the case of Remicade® (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 (18,37).

There may also be doubts, particularly among clinicians, about efficacy in the absence of clinical trial data for indications approved by use of extrapolation (3,19,37). The EMA considers that "by demonstrating biosimilarity, a biosimilar can rely on the safety and efficacy experience gained with the reference medicine", which will have been in use for at least 10 years before its patent expiry (3). This means it is not necessary for a biosimilar to undergo clinical trials for all indications, since the EMA considers that, if biosimilarity has been sufficiently demonstrated based on the totality of evidence in the comparability studies, and comparable efficacy and safety has been demonstrated in trials for one therapeutic indication, that data may be extrapolated to other indications of the reference product (2,5,19,37).

Extrapolation is fundamental in reducing the number of clinical studies required, allowing biosimilars to be marketed at competitive prices (27,39). It is not a new concept, and has been widely exercised for many years, e.g. when originator biological medicines with several approved indications undergo major changes to their manufacturing processes or a re-formulation (e.g. trastuzumab IV to sub-cutaneous) (5,6,27,39,40). Biosimilars are not automatically awarded extrapolation of indications (2). This is decided on a case-by-case basis, and if EMA criteria are not adequately met, additional studies may be necessary to provide supporting data in the extrapolated indication (6,21). Requirement for clinical data for all indications would effectively raise the regulatory standards above those applied for major manufacturing changes for innovator products (39).

Over time, concerns about extrapolation have been largely allayed with confidence in biosimilars gained from their use in clinical practice, alongside presentation of the results of switching studies (18,41). For instance, infliximab biosimilars were granted approval by the EMA for use in gastroenterology indications based on clinical data extrapolation from studies in rheumatoid arthritis (18,37). Gastroenterologists were concerned by the lack of published data for infliximab biosimilars in inflammatory bowel disease, and the British Society of Gastroenterology (BSG) initially issued a statement (2014) advising caution and avoidance of actively switching patients until further data were available (6,18). Two years later (2016), the BSG released a new statement advising members that there was now sufficient evidence to demonstrate the comparable safety and clinical efficacy of the infliximab biosimilars to the reference drug (Remicade), and that switching from Remicade to a biosimilar was also safe and effective (41).

To date, all biosimilars approved in the EU have performed as expected in all indications, including extrapolated indications (5,37,40).

- **Interchangeability**

  The issue of biologic and biosimilar interchangeability is an area that continues to cause confusion, not helped by variation in definitions and guidance provided to clinicians (12,27,42). EMA evaluations of biosimilars do not include recommendations on whether a biosimilar should be used interchangeably with its reference medicine, and devolves these decisions to the individual EU member states (5,25). This has resulted in inconsistent country-specific rules on interchangeability (42). Although no clear definition or position statement has been offered by the MHRA, it has been suggested that interchangeability in the UK context refers to pharmacy being able to automatically substitute any biosimilar product for the originator or another biosimilar without informing the prescriber as the expected clinical outcome is the same (12,43). Recent draft guidance from US regulators (the FDA) on demonstrating interchangeability of biosimilars offers a similar definition (44,45). In this context, since automatic substitution is not permitted in the UK, and the MHRA recommend biosimilars are prescribed by brand name in order to ensure that this does not occur, biosimilars cannot be considered interchangeable (2,12,23,28,46).
However the British Biosimilars Association argues that, if applying the European Commission definition of interchangeability "the medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient on the initiative, or with agreement of the prescriber", there is no reference to automatic substitution (7). Therefore biosimilars can be considered as interchangeable since the regulator has determined, through the approval process, that they have the same clinical effect in a given clinical setting to the reference medicines. The European Association of Hospital Pharmacists also supports the view that a reference product and its biosimilar(s) are interchangeable, as are a biosimilar product and other biosimilar(s), and therefore can be switched (33).

Whichever definition is applied would not preclude switching patients to a biosimilar, as long as the decision to switch involves the prescriber in consultation with the patient (5,12).

- **Safety**

With regards to concerns about safety, the regulatory processes outlined above should again provide assurance that a biosimilar can be considered as safe as the reference medicine (21,27). By demonstrating high similarity to the reference biological, a biosimilar can rely on the proven safety of that product (5,25). The clinical studies must demonstrate similar type and incidence of adverse reactions to the reference medicine, and not identify any new safety concerns (37). Nonetheless, there will inevitably be gaps in the evidence, since regulatory trials do not provide long-term safety data, and are not sufficiently powered to detect rare, unexpected adverse effects (13). Patients included in the trials may not reflect “real world” patients (29). The robustness of post-marketing safety monitoring and engagement of manufacturers in pharmacovigilance processes and provision of product support services and risk minimisation materials (e.g. patient alert cards, educational material) should therefore be assessed by healthcare professionals and commissioners when considering switching patients to a biosimilar (5,8,13,23).

As with other medicines, all biosimilars authorised by the EMA will be required to adhere to a post-marketing risk management plan, and this will typically include an obligation to search for switch-related adverse events (5,33). NICE support use of patient registries to collect safety data which are often industry funded (8,13,15). All newly authorised biosimilars will have ‘black triangle’ (▼) status in the UK, so any suspected adverse drug reactions (ADRs) should also be reported through the Yellow Card Scheme (8,15,24). In accordance with European legislation, the MHRA request provision of the brand name and specific batch number on any ADR report for a biological medicine (5,9,15,27,28,). For this reason it is important, if a patient is switched from one biological medicine to another with the same active substance, to prescribe by brand name, and to record the brand name and batch number at all stages of patient care, including supply and administration (5,27). Practical safety considerations will also need to be taken into account before switching patients, since small differences, e.g. injection devices, administration technique, product labelling, may be more significant in some patients and some patients may be less able to adapt when switching (13,23). To help with this, UKMi publish ‘in-use safety assessments’ for each biosimilar launched in the UK, available via www.sps.nhs.uk (8).

A key safety concern to be addressed is immunogenicity (12,26,37). This is a rare complication of treatment with all biological medicines, since they possess an intrinsic ability to trigger an immune response (5,14). It may result in adverse effects of an immune nature (e.g. injection-site reactions) and/or loss of response to the medicine through the formation of anti-drug antibodies (ADA’s). Usually there will be no clinical consequences of an immune response to a biological medicine, especially since formation of ADA’s could be transient (5). Severe reactions are very rare.

At the present time, analytical techniques are not able to reliably predict immunogenicity, so regulatory
procedures must be relied on (47). The EMA require a biosimilar to demonstrate that it is equally or less immunogenic than the reference product, and will not approve products with an inferior immunogenic profile (7,27). However, there may still be concern, since switching studies are not required for regulatory approval, that data are insufficient to assess immunogenic response when switching (11,16). So clinicians and patients may be reassured that the risk of a harmful immunogenic reaction (adverse effects or loss of response) after switching is minimal (5,7,27). To provoke a strong immune response, a biosimilar would require a new T-cell epitope. This is highly unlikely since biosimilars must have the same amino acid sequence as their originators, thus should also have the same T-cell epitope (7). Other factors that might also contribute to immunogenicity, such as aggregation, impurities, misfolding and certain glycan variants are also well understood and tightly controlled, further controlling immunogenicity. The EMA “requires that the impurity profile and the nature of excipients of the biosimilar itself do not give rise to concern”.

It is reassuring that to date, with over 400 million patient days of experience, the EU safety monitoring system has not identified any relevant differences in the nature, severity or frequency of adverse effects between biosimilars and reference medicines (5,27). None of the biosimilars approved in the EU to date has been withdrawn or suspended for safety or efficacy reasons (5). Evidence after manufacturing changes, and from many years of patients switching between originator biological medicines within a therapeutic class (e.g. TNF-alpha inhibitors, low molecular weight heparins), as well as the ever-increasing experience from switches to biosimilars in clinical practice, and data from switching studies, also provides no indication that switching itself can induce immunogenicity or other adverse effects (5,7,10,14).

Switching Studies

Overall, data on the effects of switching biologics from clinical and real world studies are accumulating, providing valuable insights into efficacy, safety and immunogenicity (48). Although switch studies are not essential for a biosimilar to receive marketing authorisation in the EU, development programs of a number of biosimilars have included switch studies, often as follow-up in long-term extension studies (10,48). Data from these are published in the product assessment reports (EPARs) on the EMA website (10).

The current body of data is reassuring but, with notable weaknesses and heterogeneity in study designs, remains insufficient to fully instil confidence in switching (11,16). There is discussion in the medical literature about the ideal trial design to provide robust data on switching and reflect the expected real-world usage of biosimilars in which patients may repeatedly switch between the originator and one or more biosimilars, as well as between biosimilars (11). It has been suggested that trials would need to be randomised, controlled multiple-switch designs, and include suitable treatment intervals before switches, adequate sample sizes, informative endpoints, and assessment of ADAs. However the feasibility and benefit of such studies may be questionable (10). The US medicines regulators (the FDA) have published guidance for industry on information required to achieve a distinct ‘interchangeable’ designation for biosimilars, stipulating a trial incorporating at least three switches (45,16,48). To date, the FDA has not designated any biosimilar product as ‘interchangeable’ and there are no plans to create a similar ‘interchangeable’ designation for biosimilars in the EU (10,11).

Some of the key published switching studies are summarised in the table below. N.B. This is a rapidly evolving area, and it will be important to provide the latest evidence and treatment guidance to patients and prescribers to support them in their decision-making (49).
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<th>Study</th>
<th>Indication</th>
<th>Treatment</th>
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<tr>
<td>Jørgensen et al 2017 [NOR-SWITCH]</td>
<td>RA, SpA, PsA, UC, CD, Ps</td>
<td>Double-blind RCT across 40 centres in Norway. Patients (n=482) maintained on originator infliximab or switched to biosimilar CT-P13</td>
<td>Disease worsening similar between maintenance vs. switch groups; 26% vs. 30%; adjusted risk difference - 4.4% [95% CI = -12.7 to 3.9]. CT-P13 non-inferior to originator.</td>
<td>Frequency of adverse events (AEs) similar between groups.</td>
<td>Similar frequency of ADAs observed between maintenance vs. switch groups; 11% vs. 13%.</td>
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<td>Yoo et al 2016 [PLANETRA extension]</td>
<td>RA</td>
<td>Open-label follow-up study over 102 weeks. Patients (n=302) switched from originator infliximab to biosimilar CT-P13, or maintained on biosimilar CT-P13.</td>
<td>Response rate similar between maintenance vs. switch groups; 71.7% vs. 71.8% [95%CI= -10 to 10] for ACR20, 48.0% vs. 51.4% for ACR50 [95%CI= -15 to 8], 24.3% vs. 26.1% for ACR70 [95%CI= -12 to 8].</td>
<td>Frequency of AEs similar between maintenance vs. switch groups; 53.5% vs. 53.8%.</td>
<td>Similar frequency of ADAs observed between maintenance vs. switch groups; 40.3% vs. 44.8% (p=0.48).</td>
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<td>Park et al 2017 [PLANETAS extension]</td>
<td>AS</td>
<td>Open-label follow-up study over 102 weeks. Patients (n=174) switched from originator infliximab to biosimilar CT-P13, or maintained on biosimilar CT-P13.</td>
<td>Partial remission rates similar between maintenance vs. switch groups; 80.7% vs. 76.9% for ASAS20 (p=0.506), 63.9% vs. 61.5% for ASAS40 (p=0.672), 19.3% vs. 23.1% for ASAS PR (p=0.275).</td>
<td>Lower rate of AEs in maintenance vs. switch group; 48.9% vs. 71.4% (mainly mild to moderate AEs)</td>
<td>Similar frequency of ADAs observed between maintenance vs. switch groups; 23.3% vs. 27.4% (p=0.60).</td>
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<td>Glintborg et al 2017 [DANBIO]</td>
<td>RA, SpA, PsA</td>
<td>Nationwide switch of Danish patients (n=802) from originator infliximab to biosimilar (Remsima, Disease activities similar 3 months before and after switch. Lower adjusted retention rate in CT-P13-37 patients (4.6%) withdrew due to AEs.</td>
<td>Disease activities similar 3 months before and after switch. Lower adjusted retention rate in CT-P13-</td>
<td>No difference in ADA positivity from baseline reported at 6 months post switch.</td>
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<tr>
<td>Study Authors and Year</td>
<td>Disease/Condition</td>
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<tr>
<td>Glintborg et al 2017a [DANBIO]</td>
<td>RA, SpA, PsA</td>
<td>Nationwide switch of Danish patients (n=1548) from originator etanercept to biosimilar (Benepali, SB4)</td>
<td>Disease activity largely unchanged 3 months pre vs. 3 months post switch. Disease flare pre/post switch was 8%/13% (RA), 9%/13% (PsA), 5%/5% (SpA). 129 patients (9%) stopped SB4 during 5 months follow-up.</td>
<td>42 patients (2.7%) withdrew due to AEs.</td>
<td>Not reported.</td>
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<tr>
<td>Griffiths et al 2017 [EGALITY]</td>
<td>Ps</td>
<td>PIII double-blind RCT. Patients (n=531) received 12 weeks of originator etanercept (ETN) or biosimilar (Erelzi, GP2015), then randomised to maintenance ETN/GP2015, or to undergo a sequence of 3 treatment switches between ETN and GP2015 to week 30, then maintained on final product until week 52.</td>
<td>Similar PASI75 response rates between GP2015 vs. ETN at week 12; treatment difference = -2.3 (73.4% vs. 75.7%; 95%CI = -9.85 to 5.30). Mean PASI scores and % changes comparable between maintenance and switch groups from baseline to week 52.</td>
<td>Similar incidence of ≥1 TEAEs up to week 52 between GP2015 (59.8%) vs. ETN (57.3%). Comparable safety profiles in switching treatments.</td>
<td>Overall low incidence of ADAs, all non-neutralising, reported in 5 patients on ETN during first 12 weeks, and 1 patient in switched ETN group, who had been on GP2015 for 12 weeks at time of finding (week 36).</td>
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<tr>
<td>Smolen et al 2017</td>
<td>RA</td>
<td>PIII double-blind RCT. After 54 weeks of treatment with originator infliximab (IFX) or</td>
<td>Efficacy sustained and comparable across all 3 treatment groups. ACR20 responses weeks 54 to 78</td>
<td>Similar rates of ≥1 TEAE; 36.2% in IFX/SB2 switch group, vs. 35.6% in maintenance IFX group.</td>
<td>Newly reported ADAs from week 54: 14.6% in IFX/SB2 group, vs. 14.9% in maintenance IFX group, vs.</td>
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<td>Weinblatt et al 2016</td>
<td>RA</td>
<td>PIII double-blind RCT. After 24 weeks of treatment with originator adalimumab (ADL) or biosimilar (Imraldi, SB5), patients (n=508) randomised to maintenance ADL (n=129), or SB5 (n=254) or switched from ADL to SB5 (n=125).</td>
<td>ACR20 responses comparable across all 3 treatment groups; 76.9% in maintenance SB5 group vs. 81.1% in ADL/SB5 switch group vs. 71.2% in maintenance ADL group. Change of modified total Sharp score comparable; 0.17 in maintenance SB5 group vs. 0.25 in ADL/SB5 switch group vs. 0.50 in maintenance ADL group. Similar rates of ≥1 TEAE; 32.3% in maintenance SB5 group, vs. 37.6% in ADL/SB5 switch group, vs. 33.1% in maintenance ADL group. Similar rates of ≥1 SAE; 2.4% in maintenance SB5 group, vs. 3.2% in ADL/SB5 switch group, vs. 3.1% in maintenance ADL group. Incidence of ADAs: 15.7% in maintenance SB5 group, vs. 16.8% in ADL/SB5 switch group, vs. 18.3% in maintenance ADL group.</td>
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<td>Emery et al 2017</td>
<td>RA</td>
<td>Open-label extension study following double-blind 52-week RCT. Patients (n=245) switched from originator etanercept (ETN) to biosimilar (SB4, Benepali) or maintained on biosimilar and assessed up to week 100.</td>
<td>ACR20 response rates sustained and comparable; 77.9% in maintenance SB4 group and 79.1% in ETN/SB4 switch group. Similar rates of TEAEs; 47.6% in maintenance SB4 group and 48.7% in ETN/SB4 switch group. 1 patient per group developed non-neutralising ADAs.</td>
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<td>Medicines Q&amp;As</td>
<td>Hadjiyianni et al. 2016</td>
<td>T1D, T2D</td>
<td>Analysis of subgroup of patients with T1D (n=452) or T2D (n=299) reporting prestudy use of originator insulin glargine (IGlar) in key PIII trials of insulin glargine biosimilar (Abasaglar, LYIGlar). T1D: 218 patients switched to LYIGlar and 234 maintained on IGlar over 52 weeks. T2D: 154 patients switched to LYIGlar and 144 maintained on IGlar over 24 weeks.</td>
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<tr>
<td>Park et al 2017a</td>
<td>RA</td>
<td>Open-label extension study following double-blind Phase I RCT. Compared efficacy and safety over 24 weeks of patients switched from originator rituximab (RTX) to biosimilar CT-P10 (n=20), to those who received CT-P10 from the</td>
<td>All efficacy endpoints comparable between maintenance and switch groups with no statistically significant differences (p≥0.05).</td>
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<tr>
<td>Razanskaite V et al. 2017</td>
<td>UC, CD</td>
<td>Service evaluation at a UK hospital of patients (n=143) switched from originator infliximab to biosimilar CT-P13</td>
<td>Mean IBD-control-8 score improved from 10.4 to 11.2 [p = 0.041]. No significant difference in drug persistence between biosimilar and originator [p = 0.94]</td>
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RA=rheumatoid arthritis; SpA=spondyloarthritis; PsA=psoriatic arthritis; UC=ulcerative colitis; CD=Crohn’s disease; Ps=plaque psoriasis; AS=ankylosing spondylitis; T1D=Type 1 Diabetes mellitus; T2D=Type 2 Diabetes mellitus; TEAE = treatment-emergent adverse effect; SAE = serious adverse event; ADA = anti-drug antibody; FPG = fasting plasma glucose
Summary

- Biological medicines are highly complex molecules derived from living cells or organisms.
- 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’ or originator).
- Since biosimilars are typically available at a reduced price to the reference medicine, their use has the potential to offer the NHS considerable cost savings and widen patient access to innovative treatments.
- An NHS England commissioning framework outlines aims to increase uptake of biosimilars to ensure patients are prescribed the best value biological medicine.
- With over 10 years clinical experience across the EU, confidence in the use of biosimilars has grown, particularly in treatment-naive patients, but concerns may remain about switching patients established on a biological medicine to a biosimilar.
- Since automatic substitution of prescribed medicines at pharmacy level is not permitted in the UK, any decision to switch should involve the prescriber in consultation with the patient.
- This Q&A discusses reasons for switching and endeavours to address potential concerns for patients and clinicians, particularly those related to possible differences in quality, efficacy and safety of the biosimilar, and interchangeability with the reference product.
- Data on the effects of switching biologics from clinical and real world studies are accumulating, and a table is presented summarising some of the key published switching studies.
- The majority of studies investigate a single switch from the reference medicine to a biosimilar. Data on multiple switches, i.e. switching back and forth between the originator and a biosimilar, and on switching from one biosimilar to another, are limited.

Limitations

The table of switching studies presented in this Q&A is not comprehensive, and contains only a small sample of key studies published in recent years.

References


48. Toussirot E, Marotte H. Switching from originator biological agents to biosimilars: what is the evidence and what are the issues? RMD Open 2017; 3:e000492. doi:10.1136/rmdopen-2017-000492


Medicines Q&As

Date Prepared
31st August 2017

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Date of check
7th February 2018

Search strategy
- Medline 1946-July Week 3 2017 (via Ovid): exp *Biosimilar Pharmaceuticals/ (limited to human, English language and review articles, yr=2014-current)
- Embase 1996-2017 week 31 (via Ovid): exp biosimilar agent/ (limited to human and English language and yr="2014-Current" and "review")
- NHS England https://www.england.nhs.uk/
- PrescQIPP. Accessed via www.prescqipp.info
- Diabetes UK. Accessed via https://www.diabetes.org.uk/
- British Association of Dermatologists. Accessed via www.bad.org.uk
- British Society of Gastroenterology. www.bsg.org.uk

Available through Specialist Pharmacy Service at www.sps.nhs.uk