Biosimilar infliximab: a successful managed switch programme in people with inflammatory bowel disease

A managed programme of switching all 143 people with inflammatory bowel disease (IBD) cared for at Southampton General Hospital from originator infliximab (Remicade) to biosimilar infliximab (Inflectra) was highly acceptable to patients, clinicians, commissioners and other stakeholders. There was no evidence of any difference in terms of laboratory parameters, adverse effects or drug persistence. The drug acquisition costs reduced by £40,000–60,000 per month, which allowed an investment in care for people with IBD that may have contributed to the improvement seen in some patient-reported outcome measures. Use of biosimilar infliximab in IBD is in line with NICE’s position statement on evaluating biosimilar medicines and NHS England’s programme of work on the appropriate use of biosimilar medicines. Across England, there is still significant variation in the use of biosimilar infliximab – the median use as a proportion of all infliximab in January 2017 was about 79% but varied from more than 95% in 21 Trusts to zero in 7 Trusts.

Overview and current advice

A biosimilar medicine is a biological medicine which is highly similar to another biological medicine already licensed for use and which has been shown not to have any clinically meaningful differences from the originator (reference) biological medicine in terms of quality, safety and efficacy. Biosimilar medicines have the potential to offer the NHS considerable cost savings and widen the access to innovative medicines.

In the development of a biosimilar medicine, there is no requirement to demonstrate clinical benefit to patients per se, as this has been shown for the reference biological medicine. Instead, biosimilars undergo a comprehensive regulatory process which demands extensive comparability studies that demonstrate similarity to the reference biological medicine. 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.

In September 2013, the EMA authorised a biosimilar version of infliximab (CT-P13) under 2 brand names: Inflectra (Hospira UK Limited) and Remsima (Celltrion Healthcare Hungary Kft; marketed in the UK by Napp Pharmaceuticals Limited). The pharmaceutical form, strength, therapeutic indications and dosing regimens of Inflectra and Remsima are the same as those of the reference medicine, Remicade. The clinical data demonstrating the similarity between CT-P13 and Remicade consisted of 2 main randomised controlled trials (RCTs):
A 30-week, multicentre, double-blind, parallel group pharmacokinetic (phase 1) RCT in 250 people with active ankylosing spondylitis (PLANETAS, Study CT-P13 1.1; ClinicalTrials.gov Identifier: NCT01220518).

A 30-week, multicentre, double-blind, parallel group efficacy and safety (phase 3) RCT in 606 people with active rheumatoid arthritis despite treatment with methotrexate (PLANETRA, Study CT-P13 3.1; ClinicalTrials.gov Identifier: NCT01217086).

In the UK, the MHRA recommends that 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 reference biological medicine rests with the responsible clinician in consultation with the patient.

Infliximab is recommend as an option for people with inflammatory bowel disease in 3 NICE technology appraisals: Infliximab for acute exacerbations of ulcerative colitis; Infliximab and adalimumab for the treatment of Crohn’s disease and Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy. The recommendations in these pieces of guidance also apply to biosimilar products of infliximab that have a marketing authorisation allowing the use of the biosimilar for the same indication.

In February 2016, the British Society of Gastroenterology published guidance on the use of biosimilar infliximab (Inflectra and Remsima) in inflammatory bowel disease. This recommends that there is sufficient evidence to recommend that people 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).

The NHS England Medicines Optimisation Dashboard indicates that, in January 2017 (the most recent data available), use of biosimilar infliximab by hospital Trusts as a proportion of all infliximab varied considerably across England. Median use of biosimilar infliximab as a proportion of all infliximab was about 79% but the interquartile range was from 44% to 93%. Biosimilar use was more than 95% in 21 hospital Trusts but 7 Trusts for which data were available used only originator infliximab.

A NICE key therapeutics topic on biosimilar medicines summarises the evidence-base for biosimilar medicines. NICE has also published an adoption resource introducing biosimilar versions of infliximab: Inflectra and Remsima to help manage the introduction of biosimilar medicines into care pathways safely and effectively. See also the NHS England publication, What is a biosimilar medicine? and the NHS publication Answers to commonly asked questions about biosimilar versions of infliximab for more information.

New evidence

Razanskaite et al (2017) report the outcomes of a managed switching programme from Remicade to biosimilar infliximab, CT-P13 (Inflectra), in people with inflammatory bowel disease (IBD) cared for at Southampton General Hospital.

The switch programme was designed with input from all stakeholders, including the local IBD patient panel, gastroenterologists, pharmacists and the IBD nursing team. The programme was funded through a gain share agreement with the local clinical commissioning groups (CCGs) that also funded developments in the IBD service, including a new IBD specialist nurse post, a 0.5 whole time equivalent (WTE) clerical post, a 0.2 WTE pharmacist post and a 0.2 WTE dietitian post. This amounted to about 12% of the projected gross savings. All savings net of the investment were shared equally between the hospital Trust and the CCGs.
The switch programme began in April 2015 and everyone with IBD treated with infliximab was offered the opportunity to participate. All 143 people (118 with Crohn’s disease, 23 with ulcerative colitis and 2 with unclassified IBD) agreed to switch to the biosimilar. The median duration of illness was 6 years (range 0–36 years) and the median number of originator infliximab infusions received before switching was 10 (range 1–67). Data were collected on clinical outcomes, haematological parameters, serum drug and drug-antibody levels, drug persistence (time on treatment), safety and drug acquisition costs.

Patient-reported disease control data were collected from 93 (65%) people before and after switching to biosimilar infliximab. The median IBD-Control-8 score increased from 11/16 at the switch to 14/16 at the third dose (p=0.041), suggesting an improvement in disease control. The authors speculate on whether this was influenced by the increased monitoring associated with the switch and the additional support from the extra IBD specialist nurse time. There was no statistically significant difference in mean IBD-Control visual analogue score at these time points (72.5 and 72.4 respectively, p=0.65).

Routine haematological test results were available for 126 (88%) people before switching and after at least 3 doses of biosimilar infliximab. There were no statistically significant differences in mean C-reactive protein, albumin levels, platelet count or white cell count. Mean haemoglobin levels increased after the switch, from 132.4 g/L to 135.2 g/L, p=0.004.

Serum infliximab trough and anti-drug antibody levels were measured in 70 people before switching and after 3–5 doses of biosimilar infliximab. There were no statistically significant differences in infliximab trough levels, number of people with anti-drug antibodies and mean anti-drug antibody levels.

Two people were switched back to originator infliximab at their request. One person was on concomitant mercaptopurine and had abnormal liver enzymes and the other person had non-specific flu-like symptoms. Drug persistence in the switch cohort from April 2015 to March 2016 was compared with drug persistence in the cohort of all people with IBD (n=120) treated with originator infliximab in the previous 12 months. There was no statistically significant difference between the 2 cohorts in duration of treatment and if treatment was withdrawn it was for similar reasons in both cohorts. A broadly similar pattern of treatment-emergent adverse events was reported before and after the switch.

Drug acquisition costs reduced rapidly after the switch, by £40,000–60,000 per month.

Commentary
Commentary provided by NICE

This report adds to the available data on the use of biosimilar infliximab in people with IBD. It supports the British Society of Gastroenterology guidance that that people with IBD who are in a stable clinical response or remission on originator infliximab therapy can be switched to biosimilar infliximab at the same dose and dose interval.

The report also highlights the practical and strategic issues involved in a successful managed switch programme. The NICE adoption resource on 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, releasing funds to develop other services or provide greater access to innovative and effective 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.

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**References**


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