Effective Prescribing Programme - optimising the safe and effective use of biological medicines

Case studies
Introduction

These case studies outline the experiences, challenges and lessons learned to date by NHS Boards that have invested in review clinics in Rheumatology and Gastroenterology to:

- Switch existing patients from an originator biological medicine to the biosimilar version (NHS Grampian and NHS Highland).
- Reduce dose in stable biologic patients (NHS Greater Glasgow and Clyde and NHS Lothian).

Their experiences demonstrate that it is possible to maintain the highest level of care for the patient and make financial efficiencies by adopting a shared decision-making approach between clinician and patient.

Each case study is unique; however there are some key learning points:

- Clinical and service engagement with key stakeholders and decision makers is essential. This can support the initial case for management and agreement of the approach for the service. Success requires strong buy-in from senior management and the clinical teams.
- Securing additional staffing resource has been central. A small amount of investment has been required in most cases in order to review, counsel and monitor patients.
- Capacity and logistics is a key issue for NHS Boards. It can be challenging to free up clinician time – be that consultant, nurse or pharmacist time – clinic space or physical rooms.
- Sustainability of the service requires robust structures in place. Currently, systems can be person dependent and, therefore, vulnerable.
- A shared decision-making approach between clinician and patient: patients have been supportive of the switch to biosimilars where there has been good communication and engagement with the healthcare team. Drug trough levels have guided clinicians as a marker of response and helped reduce patient exposure to unnecessary drug dosage.
- There is an essential requirement to ensure that mechanisms are in place for support and quick access back into the system.
- Data is key to delivering improvement and supporting the clinician-patient discussion in patient reviews.

We would encourage NHS Boards to consider these case studies, the rich learning they offer and any applicability to your local NHS Board.
NHS Grampian
Biological case study
This case study outlines some of NHS Grampian’s early experiences of switching patients from an originator biologic medicine to a biosimilar.

NHS Grampian started a proactive switching programme in August 2016 to switch existing rheumatology patients receiving the etanercept originator product to the biosimilar version. There are currently 245 adult rheumatology patients receiving etanercept.

**Key drivers**

Like other NHS Boards, NHS Grampian is exploring ways to make financial efficiencies. Biosimilar medicines were identified as a key area where potential savings could be realised.

NHS Grampian has a favourable history of supporting ‘invest to save’ approaches. Biosimilar medicines were identified as a suitable candidate – usage and uptake rates are readily quantifiable and there are guaranteed savings for each patient switched.

The British Society for Rheumatology issued a position statement supporting the use of biosimilar medicines in February 2015. The Rheumatology team viewed the use of biosimilar medicines as a desirable step given the procurement savings that could be obtained.

There was an acceptance that in clinical terms the biosimilar product should deliver the same therapeutic benefits seen with the originator product. They were, therefore, supportive of a process to switch from originator etanercept to the biosimilar in existing rheumatology patients as well as initiating biosimilar etanercept for new patients starting treatment.

The Rheumatology team was aware of the success of infliximab switching in gastroenterology patients in Southampton. This was presented in a WebEx on biosimilar medicines in March 2016 organised by the Area Drug and Therapeutics Committee Collaborative and hosted by Healthcare Improvement Scotland.
Lessons learned

On reflection, there were three factors which contributed to successfully laying the foundations for the future switching of existing patients to the etanercept biosimilar:

- Clinical and service engagement with key stakeholders and decision-makers
- Defining the service position and agreeing how to achieve the defined outcomes
- Securing resource requirements to achieve the service position

Clinical and service engagement with key stakeholders and decision-makers

Key stakeholders, of varying degrees of seniority, came together to agree the way forward for the use of biosimilars for NHS Grampian’s rheumatology patients. Clinicians (medical, nursing and pharmacy) and the unit’s operational manager met with the medicines management and finance teams. Having all the relevant stakeholders with decision-making capability together was key to the early success. This allowed for a quick response to the identified need for additional resources to support switching existing patients.

Defining the service position and agreeing how to achieve the defined outcomes

The group first met in April 2016 with the objectives of the first meeting being to:

- Agree the service position on introducing the biosimilar medicine to new patients and switching existing patients
- Explore and agree potential routes of supply, including through community pharmacies and current homecare providers
- Agree any medicines governance arrangements, including prescribing by brand name and requirements to record batch numbers
- Identify any resource requirements to support adopting the agreed service position and maximising the pace of change
- Agree a plan to maximise the financial benefits achievable in 2016-2017 and in the future
The group agreed the service position:

- All new adult patients were to be initiated on the biosimilar
- Existing adult patients were to be switched, where possible, to the biosimilar

At the time of the first group meeting in April 2016, ten new patients had already been initiated on biosimilar etanercept. Additionally, the etanercept biosimilar is only available as a 50mg dose with a licence for those aged over 18-years-old. Currently, there are five patients in the children’s hospital on the 50mg dose who were not considered to be suitable for switching at present.

Once the clinical acceptance around the use of biosimilar etanercept was agreed, the discussion then focused on how to achieve the service position and the pace at which it could be achieved.

NHS Grampian decided to keep switching as simple as possible for patients by continuing the supply through their current homecare service provider: as patients would receive their supply exactly as before, the only change they would have to deal with was the product they receive. This would ensure that any issues related to the switch were only down to the change of product and were not confounded by changes in supply routes.

The option to revisit the supply route, perhaps through a community pharmacy model, was left on the table for the future. It was also acknowledged that setting up alternative models of supply would inevitably take longer and, therefore, reduce the possibility of early savings being achieved. There was agreement that new patients should be started on biosimilar etanercept and this could happen as soon as the contract issues had been finalised.

Switching patients could be done as they come back for six-monthly review appointments (these appointments would need to be longer) or by adding in additional clinics in order to speed up the process. A mixed model was considered to allow patients to be called back earlier.

The group also explored the ‘invest to save’ approach and identified how the potential savings accrued from using the etanercept biosimilar compared with the additional resource required to switch existing patients. They agreed that, for a small investment, savings could be substantial.

**Securing resource requirements to achieve the service position**

There was agreement that switching could not be done without additional staffing resource. Additional nursing and administrative time would be required to arrange appointments for patient review, to review patients and to counsel them on the switch and their new product. The appointments would, therefore, be longer for the patient than normal appointments. Consequently, the group agreed on an ‘invest to save’ approach.

It was noted that the drug acquisition costs, nursing support and delivery costs had been ‘unbundled’ as part of the National Procurement Agreement and would allow some of the nursing support to be taken back in-house.

Within a week of the group’s first meeting, the Deputy Director of Finance had signed off the recruitment requirements and the recruitment process for additional nursing and administrative staff for switching began.

NHS Grampian started a proactive switching programme in early August 2016.
Patient support

Early feedback from the switching programme has been positive and a high level of patient acceptability reported.

Previous conversations with patients and patient support groups in preparation for the switching programme indicated that patients understood the reasons for switching to the biosimilar medicines and that they would be willing to do so.

The Rheumatology team adapted the template biosimilar switch letters developed by the Area Drug & Therapeutics Committee Collaborative, Healthcare Improvement Scotland to fit with their local requirements.

Measuring success

Success will be measured through patient outcomes and biosimilar uptake rates.

The Rheumatology team are keen to gain experience to allow the development a robust model of care for any switch process, ensuring appropriate follow-up and use of biologics registers.

This can then be used in the future for patients currently receiving other biologic medicines when a biosimilar version becomes available. This should help accelerate and maximise the financial benefits achievable in 2016-2017 and in future years.
NHS Highland
Biological case study
Gastroenterology team experiences of switching to biosimilar drug

Since Autumn 2015, the Gastroenterology team at NHS Highland have been switching their 85 existing inflammatory bowel disease (IBD) patients receiving the infliximab originator product to the biosimilar version. This case study outlines some of NHS Highland’s experiences of switching patients to the biosimilar.

There are approximately 1,200 patients with inflammatory bowel disease registered with the NHS Highland gastroenterology service.

Key drivers

The Gastroenterology team within NHS Highland is a small, friendly and enthusiastic multi-disciplinary team which benefits from good relationships with patients. When members of the senior management team approached them in Autumn 2015 about being over budget, biosimilar medicines were an obvious area where financial savings could be made without detriment to the quality of patient care.

Agreeing the way forward

The two IBD advanced nurses and gastroenterologist met soon afterwards with members of the pharmacy and senior management teams to agree the way forward.

There was agreement to:

- Initiate all new patients on the infliximab biosimilar
- Switch existing patients, where possible, to the infliximab biosimilar

The team also agreed to switch patients from the infliximab originator product, Remicade®, to the infliximab biosimilar, Remsima® and check both infliximab drug and antibody levels.

There was no additional staff resource available for the purposes of switching patients and the two IBD advanced nurses managed the switching as part of their role.

Infliximab and antibody levels

Infliximab drug and antibody levels were checked for each patient on two occasions – pre-switch and repeated six months post-switch. New patients initiated on the biosimilar were also tested 12 weeks after the biosimilar was started.
Measuring trough drug levels and determining if patients have developed antibodies to the drug is a new area being explored to potentially improve outcomes for patients. Samples were taken locally and sent to a clinical laboratory in Exeter for testing.

**Switch template letter**

The IBD team developed a switch letter to explain to patients who were receiving infliximab about the team’s plans to change from Remicade® to Remsima®. Patients were sent the letters in advance of their next clinic appointment.

The NHS Highland team agreed that the Area Drug & Therapeutics Committee Collaborative, Healthcare Improvement Scotland could adapt their material for use nationally. As a result, two national template switch letters for patients were developed in March 2016 – one for infliximab and one for etanercept.

NHS Boards across Scotland have adapted the national switch letters to fit with their local requirements and personalised the letters with NHS Board logos, team names, contact details and other local information as appropriate.

**Switching existing patients**

Existing patients were seen at their next appointment in the infusion suite by which time they had already received the letter explaining the team’s plans to change product. Drug and antibody levels were taken at this point. The IBD nurses were available to speak to patients and reassure them, if necessary.

Thereafter, patient cases were reviewed at the weekly IBD multidisciplinary team meeting. This offered an opportunity to review and adjust patient management plans.

Patients who were not responding to treatment and had poor infliximab levels and positive antibody levels were stopped immediately. Patients for whom there was agreement to switch to the infliximab biosimilar were seen at their next clinic appointment. The situation was explained to patients at their next appointment and patients were given the opportunity to ask questions and make an informed choice.

Of the 85 existing patients:

- 62 patients were switched to the infliximab biosimilar
- 19 patients had their infliximab treatment discontinued following consideration of their overall clinical condition, response to treatment and positive antibody results
Two patients remained on the originator product – one patient was pregnant and the other patient was a complex case being managed by several consultants

One patient moved out of the NHS Highland area

One patient switched to an alternative anti TNF to fit with a change in work circumstances

**Patient engagement**

All patients who switched were comfortable with the change in their medicines due to the level of information and communication provided by the healthcare team. Patients valued the shared decision-making and appreciated decisions were not solely based on money. They were comfortable that the money saved would benefit the healthcare of other patients.

Some of the patients have been known to the team for a number of years and the team have the advantage of already benefiting from good communication with patients and a high level of trust. Patients felt the infliximab drug and antibody levels offered reassurance and the team were able to explain to patients that they are well but, as indicated by the laboratory results, not as a result of treatment with infliximab.

**Reflection**

The success of switching is down to a number of factors:

- Effective patient engagement
- Good team working within the clinical specialty
- Infliximab switch letter for patients
- Infliximab drug and antibody levels

The Gastroenterology team are now sharing their learning and experiences with the Rheumatology team as they switch their existing patients on etanercept to the biosimilar product.

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NHS Greater Glasgow and Clyde
Biological case study
Pilot consultant-led biologics dose reduction in rheumatology

NHS Greater Glasgow and Clyde is in the process of piloting a consultant-led biologics dose reduction clinic on two hospital sites – Royal Alexandra, Paisley and Vale of Leven, Alexandria.

Together, these hospitals serve around 300,000 patients - one quarter of the 1.2 million population served by NHS Greater Glasgow and Clyde.

Key drivers

There were two key drivers behind the set up of the biologics dose reduction clinic:

1. As a speciality, Rheumatology has benefited significantly from developments in biologics. Biologic drugs have been highly successful in treating rheumatic diseases, including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Patients can now expect better quality of life, reduced disability, and better pain control. However, there are also drawbacks in the form of increased risk of infection, skin cancer and notable drug costs. Clinicians reported a responsibility to ensure the effective prescribing of biologics, using judiciously and appropriately to optimise their use. It was also recognised that the review and documentation of response to biologics for patients in remission could be improved.

2. A growing evidence base indicating that dose reduction in selected groups of patients can be achieved without the deterioration of disease activity.

Preparing the business case

The business case was prepared to provide an additional consultant session per week for a period of 12 months to deliver a consultant-led dose reduction of biologics. This included an outpatient clinic twice monthly for the identification and monitoring of biologic patients.

The pilot aimed to taper biologic drugs in 10% of patients and to assess clinical response. Additionally, it sought to establish a local lab assay for detecting anti-drug antibodies (ADA) and trough drug levels.
NHS management were supportive of the proposal from the start. It was recognised that successful tapering of only a few patients would cover the expense of the additional session. Therefore, only a small amount of investment was required to deliver potentially significant savings and hopefully improve patient care. The proposal was developed and approved within three months.

**Start-up**

The additional clinic session was funded for a period of 12 months. The consultant responsible for the development of the business case would deliver the additional clinic. It was decided that the 12-month period would start with the first clinic in order to give the pilot the full amount of time to recruit patients and demonstrate effect. This meant that the preparatory work to identify and review patients for invitation to clinic was undertaken by the consultant within their existing time and prior to the pilot commencing. Administration was also absorbed by the secretary to the consultant which, on reflection, would have benefited from being included in the business case.

**Approach**

The first step in the process was to identify patients suitable to be considered for dose reduction. A list of biologic rheumatology patients was obtained for the two hospitals from prescription records. Stable patients in long-term remission were identified through case review. Patients were then contacted by letter or telephone to determine their interest in drug tapering and invited to clinic. Twice-monthly clinics were established for counselling, patient selection and to provide quick access in event of disease flare.

The majority of patients were reviewed in clinic, with a small number assessed by their own clinician, in order to identify those really suitable for dose reduction. Clinicians were supportive of the approach. The response from patients has also been positive. The vast majority of patients would prefer to take a lesser amount of drugs for the same benefit.

ADA testing of patients taking a biologic treatment was undertaken as part of routine care. It is anticipated that data analysis at the end of the pilot will determine if there are specific features which could identify a cohort of patients that would benefit from early ADA testing and any connection of ADA presence and patients able to reduce dose of biologics.
Challenges

The main challenges encountered were capacity and clinic space:

- Funding was secured for an additional clinical session; however, freeing up the time for the session was challenging. This is likely to be a common challenge for NHS Boards. If dose reduction clinics are consultant-led, then backfill may be required. To provide a sustainable service beyond the pilot, consideration is being given to recruiting a Lead Pharmacist to run the clinics working with Consultant Rheumatologists.

- Finding clinic space is a real challenge as clinic rooms are largely booked out. In the pilot, this was overcome by holding the clinic on a Friday afternoon which tends to be a quieter time in the hospital.

Initial results

Across the two hospital sites:

- 154 rheumatology patients were identified as being on biologic drugs
- 75 patients were in remission and contacted
- After seven months, 18 patients have started tapering of therapy
- Drugs tapered included etanercept (fortnightly dosing), adalimumab (3-weekly dosing) and golimumab (6-weekly dosing)
- One patient has had a flare of disease requiring re-escalation of treatment
- Cumulative cost savings over the first seven months are £19,164
- Projected savings at one year are £68,435
- The cost incurred is £10,451

The pilot would suggest that significant clinical and financial benefits could be achieved by careful selection of individuals for biologics dose reduction.

Prompt access to review in the event of flare and careful disease monitoring and scoring is essential to the success of the approach. Monitoring therapeutic drug levels is likely to play a part in this process.

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NHS Lothian
Biological case study
Pharmacist-led Biologics Dose Reduction Clinic (BDRC) in Rheumatology

NHS Lothian has gone through a process, starting in June 2015, to secure additional manpower to develop and implement a pharmacist-led Biologics Dose Reduction Clinic (BDRC) in rheumatology. This case study presents key components of the planning process and the specific challenges encountered and overcome.

The Rheumatic Diseases Unit at the Western General Hospital, Edinburgh is a joint University/NHS academic and clinical unit and is the major referral centre for patients with rheumatic diseases in South East Scotland. The unit had approximately 700 Rheumatoid Arthritis (RA) patients on anti-TNF therapy at July 2015.

Key drivers

NHS Lothian has long-term experience in using biologics in rheumatology patients. Biologic medicines have been highly successful in treating patients with rheumatic conditions. However, there are also risks associated with their use, such as an increased risk of infection. The unit has robust processes and risk management in place for the use of biologics. Based on experience within the unit and learning from elsewhere, it appeared the natural next step to consider the potential for dose reduction in those patients stable on anti-TNF therapy.

Recent literature shows that about 60% of RA patients who are stable on anti-TNF therapy may be candidates for dose reduction (van Herwaarden et al BMJ 2015). Of the patients who are potentially eligible, the dose can be reduced in 40% and treatment stopped in 20%.

This approach offered the potential to reduce burden and harm from overtreatment, prevent waste and deliver financial savings.

Making the case for change

The initial proposal for the BDRC was made to the NHS Lothian Acute Prescribing Forum (APF) in June 2015.

The Clinical Director for the Rheumatology Service in NHS Lothian advised APF members of published data showing that many patients established and stable on biologic therapy -
predominantly those with RA - were able to reduce the frequency of injections and retain control of their disease activity. Due to the high cost of biologic therapies and increasing financial pressures, this approach had the potential to improve patient outcomes and deliver cost savings for NHS Lothian.

In order to make this happen, it was recognised that additional manpower resource would be required to:

- Identify and engage with suitable patients
- Manage and supervise the dose reduction process
- Audit the programme

Funding was sought for additional pharmacy resource (0.5WTE) to backfill the Lead Pharmacist to deliver clinics and supported by a clinician (0.2WTE).

The BDRC would initially focus on anti-TNF therapy (all forms of TNF inhibitors). The indications for dose reduction being rheumatoid arthritis (RA) and ankylosing spondylitis (AS), with a view to including psoriatic arthritis (PsA) in the future.

Clinical analysis indicated 180 stable patients (of 700 patients currently) on TNF inhibitory therapy eligible for dose reduction or stopping treatment altogether.

It was anticipated that treatment could be stopped in 36 patients (20%) and dose reduction in 72 patients (40%).

For those patients on dose reduction, it was assumed that a 25% reduction in dose could be achieved for half of the dose reduction patients and 50% reduction in the other half of the dose reduction patients).

In July 2015, an Efficiency and Productivity Project Plan was submitted and approved by General Surgery Directorate to recruit on a 12-month fixed-term contract basis.

It was originally anticipated that the project would start in October 2015 and run until March 2016.
Implementation

On receiving approval to proceed, the project was driven by the Lead Pharmacist and Clinical Director for the Rheumatology Service, working with the Service Manager.

Key steps included:

- Recruitment of the 0.5WTE pharmacist to provide backfill for the Lead Pharmacist to undertake the BRDC; training and support once in post
- Development of a protocol for the clinic based on current evidence and approved by local rheumatologists
- Identification of potential patients through the locally administered database and review of individual patient electronic medical records to assess inclusion criteria
- Securing of a room to hold the clinic
- Securing of non-clinical support for the clinic to make appointments, pull case notes and prepare clinic letters
- Acquiring nursing staff support for the clinic
- Obtaining database administrative support to ensure details of each clinic visit is recorded on the local database to allow audit on patient numbers, clinical and financial outcomes

The Lead Pharmacist took responsibility to co-ordinate and meet with key managers to progress these steps concurrently with the recruitment process.

Success factors

On reflection, there were three factors critical to the successful set up of the BDRC:

- Securing additional resource to create new capacity
- Clinical engagement
- Engagement with patients

Securing additional resource to create new capacity

Patients for review are already in the system and so effectively an internal referral to the BDRC. As such, it was necessary to create new capacity to see these patients.

There was no scope for the Rheumatologists to take on an extra clinic; and to replace an existing clinic would take resource away from new appointments with a direct impact on waiting times. A pharmacist-led clinic was therefore explored; however, again, this required additional resource to backfill the Lead Pharmacist to be released to run the clinic.

Clinical engagement

From the beginning, Rheumatologists in the unit were supportive of the BDRC. Some clinicians had already started to explore dose reduction, however were not able to offer the follow-up support that the BDRC would provide. The BDRC has three clinics per week and a helpline. Clinicians were
reassured that patients requiring quick access would be scheduled an appointment that same week.

The protocol developed for the clinic was based on the criteria for dose reduction from the published data. The Clinical Director for the Rheumatology Service achieved sign off from the Rheumatology clinicians.

However, the protocol was later reviewed on the basis that some clinicians had requested notification of patients identified for dose reduction in advance of the clinic making contact. This was due to some difference in opinion on the eligibility criteria. The protocol was revised to add this step to the process.

Patient identification and engagement

The Rheumatology Unit uses a locally developed and maintained biologics database. From this, all RA patients on a biologic medicine for 12 months or more were identified and patient case notes reviewed by the Lead Pharmacist against the eligibility criteria to identify patients suitable for the BDRC.

Following clinician approval, patients were invited by letter to attend the clinic. The letter invited patients to a new clinic established to review patients on biological medicines.

It is at the clinic appointment that there is a conversation between the Lead Pharmacist and the patient on the potential for dose reduction, assessment and approach including mechanisms for quick access if required.

In the first six weeks of the clinic, all patients suitable for dose reduction (n=20) have agreed to participate in programme. Patients invited to clinic have viewed the potential for dose reduction as a positive step. This has been an honest conversation with the patient providing an approach that is good for the patient by allowing a reduction in the frequency of injections in a managed way with direct access to support if required. Equally, it is good for the NHS in making best use of limited resources, reducing waste and allowing more patients to benefit from biologics.

Challenges overcome

There were a number of challenges to the setting up of the BDRC, from the initial proposal to the first clinic being held took a period of ten months. This was a delay of six months from the original planned implementation date of October 2015.
There was a delay to the release of the funded backfill pharmacist post. Although the Efficiency and Productivity Project Plan had been approved in July 2015 to recruit on a 12 month fixed-term contract basis, further internal negotiations meant that the pharmacist post was not advertised until October 2015.

Preparatory work was undertaken by the Lead Pharmacist to prepare for the setting up of the clinic in parallel with the recruitment process. The practicality of securing a room for the clinic and administrative support was both challenging and time consuming. It was noted that different areas had different priorities and the project would have benefited from a decision being approved at Directorate level and cascaded down. A key learning point is the need for strong buy-in from senior management to support such initiatives.

**Specialist rheumatology training needs**

On recruitment of the backfill pharmacist (late January 2016), a further period of time was required to provide specialist rheumatology training and support prior to releasing the Lead Pharmacist to start the clinics. Specialist knowledge in rheumatology is uncommon in the NHSScotland pharmacist workforce. This is a real challenge in terms of succession planning and, without specialist posts being made available within NHS Boards, it is difficult for pharmacists to gain this experience. The system is therefore very person dependent and therefore quite vulnerable.

The first round of recruitment for the GP specialist to provide support for the BDRC was unsuccessful; however additional training in rheumatology was expected. In terms of learning, it is important to assume that staff recruited will not have experience in rheumatology – pharmacist or GP specialist – and therefore a period of training will be required.

**Looking forward**

The BDRC started in May 2016 and has been well received by clinicians and patients.

The model of a pharmacy-led clinic is innovative and provides a model which other areas may wish to consider.

The BDRC has not been collecting bloods for antibody testing; however this may be a development in the future if biochemistry were able to process the samples.

The results will be available in due course to report on patient numbers and clinical and financial outcomes.

It is hoped that by demonstrating a return on investment that the clinic will receive support to continue in future years. It is essential that the structure is in place to provide a sustainable service as it is not possible to absorb this type of clinic within existing resource.

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This case study was developed with Carole Callaghan, Advanced Clinical Pharmacist (Rheumatology). Carole Callaghan and Stuart Ralston worked closely to introduce a pharmacist-led biologics dose reduction clinic in Rheumatology for NHS Lothian.